Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i6.1801
*Biol. Clin. Sci. Res. J., Volume 6(6), **2025**: 1801*
Original Research Article

Effects of Inhaled Salbutamol Versus 0.9% Normal Saline on Duration of Hospital Stay in Transiennt Tachypnea of Newborn

Ayesha Anam*, Asif Javeed, Sidra Shahid, Saima Manzoor

Department of Pediatric Medicine, Ibn-E-Siena Hospital and Research Institute Multan, Pakistan
**Corresponding author`s email address:* anumayesha59@gmail.com

(Received, 14th January 2025, Accepted 15th June 2025, Published 30th June 2025)

Abstract: *Transient tachypnea of the newborn (TTN) is a common cause of respiratory distress in neonates, often requiring prolonged hospitalization and oxygen therapy. Enhancing lung fluid absorption using beta-agonists like salbutamol may reduce disease duration and hospital stay.* ***Objective:*** *To compare the effects of inhaled salbutamol versus 0.9% normal saline on the duration of hospital stay and oxygen therapy in neonates diagnosed with TTN.* ***Methods:*** *This randomized controlled trial was conducted at the department of Pediatric Medicine in the Ibn-e-Siena Hospital Multan from November 2023 to November 2024 and included 60 term or late preterm neonates with clinical and radiographic evidence of TTN. Participants were randomly assigned to receive either a single dose of inhaled salbutamol (0.15 ml/kg in 4 ml saline) or 4 ml of 0.9% saline via nebulization. Respiratory parameters were monitored, and the primary outcome was duration of hospital stay. Secondary outcomes included duration of oxygen therapy and improvements in respiratory rate and oxygen saturation. Data were analyzed using SPSS version 23.0, and an independent t-test was applied. A p-value ≤ 0.05 was considered statistically significant.* ***Results:*** *The mean duration of oxygen therapy was significantly lower in the salbutamol group (7.13 ± 2.16 hours) compared to the control group (11.67 ± 5.97 hours; p < 0.001). The mean duration of hospital stay was also shorter in the salbutamol group (3.33 ± 1.16 days) than in the control group (4.90 ± 1.49 days), although the difference was not statistically significant (p = 0.229). Baseline characteristics such as gestational age, birth weight, and maternal age were comparable between the groups.* ***Conclusion:*** *Inhaled salbutamol is effective in reducing the duration of oxygen therapy in neonates with TTN. Although not statistically significant, it may also contribute to shorter hospital stays. This intervention may be particularly beneficial in resource-constrained settings. Further larger-scale studies are warranted.*

Keywords: Beta-agonist, Hospital stay, Inhaled salbutamol, Neonates, Oxygen therapy, Randomized controlled trial, Transient tachypnea of the newborn (TTN)

[***How to Cite:*** Anam A, Javeed A, Shahid S, Manzoor S. Effects of inhaled salbutamol versus 0.9% normal saline on duration of hospital stay in transiennt tachypnea of newborn. *Biol. Clin. Sci. Res. J.*, **2025;** 6(6): 133-135. doi: https://doi.org/10.54112/bcsrj.v6i6.1801]

Introduction

Transient tachypnea of the newborn (TTN), also referred to as "wet lung syndrome," is one of the most common causes of respiratory distress in neonates, particularly among term and late preterm infants. It is characterized by delayed absorption of fetal lung fluid, leading to increased work of breathing, tachypnea, and, in some cases, hypoxia. The estimated incidence of TTN ranges from 4 to 5.7 per 1,000 live births globally, with higher rates observed in cesarean deliveries and male neonates (1).

Physiologically, normal fluid clearance in the lungs occurs via epithelial sodium channels (ENaCs), which facilitate sodium and water reabsorption. In TTN, these channels remain underactive due to immaturity or hormonal factors, leading to impaired lung fluid clearance and subsequent accumulation in the alveoli (2). This results in poor alveolar ventilation and gas exchange. The clinical manifestation typically appears within the first few hours after birth and usually resolves within 72 hours. However, in some cases, it may require prolonged hospitalization and oxygen support, leading to increased healthcare costs and parental anxiety (3).

In Pakistan, neonatal respiratory disorders account for a significant proportion of NICU admissions, and TTN is frequently observed in term neonates born by elective cesarean section (4). The standard management of TTN remains supportive, involving supplemental oxygen, close monitoring, and delayed initiation of oral feeding. However, pharmacologic agents that can accelerate alveolar fluid reabsorption may offer potential advantages in reducing the duration of respiratory symptoms and hospital stay (5). Salbutamol, a short-acting β2-adrenergic agonist, has been shown to activate sodium channels in alveolar epithelial cells and stimulate the absorption of lung fluid in experimental models (6). This has led to the hypothesis that inhaled salbutamol may be beneficial in conditions like TTN, where fluid retention is the core issue. Several clinical trials and pilot studies have explored the use of nebulized salbutamol in neonates with TTN and have reported promising outcomes, including reduced oxygen requirement and earlier resolution of symptoms (7, 8). However, evidence remains inconclusive, and the use of salbutamol has not been widely adopted into routine neonatal care. In contrast, normal saline nebulization is often used as a placebo or supportive measure without pharmacologic effects. Comparing salbutamol with normal saline helps delineate the true therapeutic potential of β2-agonists while minimizing placebo bias. Given the scarcity of region-specific data and the variability in neonatal care practices in low-resource settings such as Pakistan, it is essential to investigate context-specific interventions that may optimize clinical outcomes and reduce NICU burden.

Thus, the present study aimed to compare the effects of a single dose of nebulized salbutamol with 0.9% normal saline on the duration of hospital stay in neonates diagnosed with TTN. This study also assessed secondary outcomes including the duration of oxygen therapy, respiratory rate improvement, and oxygen saturation changes, aiming to provide evidence for safe and effective pharmacologic intervention in neonatal respiratory management in our region.

Methodology

This randomized controlled trial was conducted at the department of Pediatric Medicine in the Ibn-e-Siena Hospital Multan from November 2023 to November 2024 after approval from the institutional ethical review committee. The study aimed to compare the effect of inhaled salbutamol versus 0.9% normal saline on the duration of hospital stay in neonates diagnosed with transient tachypnea of the newborn (TTN). A

total of 60 neonates fulfilling the predefined inclusion and exclusion criteria were enrolled through non-probability purposive sampling.

Eligible neonates included term or late preterm newborns with gestational age greater than 34 weeks, presenting within a few hours of birth, and diagnosed clinically and radiologically with TTN. The clinical criteria included persistent tachypnea (respiratory rate >60/min), signs of respiratory distress such as nasal flaring, grunting, and use of accessory muscles, along with radiographic findings consistent with TTN. Radiological evidence required at least one of the following features: perihilar congestion or streaking, fluid in the interlobar fissures, pulmonary edema, fluffy bilateral infiltrates, or hyperinflated lungs. Neonates of either gender were included.

Exclusion criteria were strictly followed to reduce confounding factors. Neonates with major congenital anomalies (e.g., tracheoesophageal fistula, congenital diaphragmatic hernia, congenital heart defects), those diagnosed with meconium aspiration syndrome (evidenced by meconium-stained skin and characteristic chest radiograph findings), respiratory distress syndrome (with reticulogranular pattern), and birth asphyxia (defined as APGAR score <5 at birth) were excluded.

Upon enrollment, neonates were randomly assigned to one of two intervention groups using sealed opaque envelopes labeled Group A and Group B. Randomization was achieved by draw method to ensure allocation concealment. Group A (intervention group) received a single dose of inhaled salbutamol at a dose of 0.15 ml/kg diluted in 4 ml of 0.9% normal saline via nebulization. Group B (control group) received 4 ml of 0.9% normal saline alone via nebulization. The nebulization was administered within the first few hours of life and completed over approximately 10 minutes using a standard neonatal nebulizer setup.

All enrolled neonates received standard supportive care, including oxygen supplementation, intravenous fluids, and thermal regulation as per NICU protocol. Clinical parameters including respiratory rate, work of breathing, and oxygen saturation (SpO_2) were recorded before nebulization and at 1 hour, 4 hours, and 6 hours post-nebulization. The duration of oxygen therapy (in hours) and total hospital stay (in days) were recorded as outcome measures.

Data analysis was performed using IBM SPSS Statistics version 23. The normality of distribution for continuous variables such as gestational age, birth weight, maternal age, duration of oxygen therapy, and hospital stay was assessed using the Shapiro–Wilk test. Quantitative variables were summarized as mean ± standard deviation (SD) or median and range, depending on distribution. Categorical variables like gender and mode of delivery were expressed as frequencies and percentages.

The primary outcome (duration of hospital stay) was compared between the two groups using the independent samples t-test. Secondary outcomes, including duration of oxygen therapy and differences in respiratory parameters, were also analyzed. A p-value of ≤0.05 was considered statistically significant. To control for confounding factors, post-stratification analysis was conducted based on variables like gestational age, birth weight, maternal age, and gender, followed by t-tests within each stratum.

Results

A total of 60 neonates diagnosed with transient tachypnea of the newborn (TTN) were included, with 30 participants in the salbutamol group and 30 in the normal saline (control) group. The mean gestational age was 37.38 ± 1.44 weeks, and the average birth weight was 2740.00 ± 240.20 grams. The mean maternal age was 25.63 ± 2.66 years. The average duration of oxygen therapy was 9.40 ± 5.01 hours, and the mean duration of hospital stay was 4.12 ± 1.54 days. Table 1 presents the overall descriptive statistics of the sample.

Shapiro-Wilk test indicated that birth weight followed a normal distribution (p = 0.232), while gestational age (p = 0.010), maternal age (p = 0.003), and duration of oxygen therapy (p < 0.001) deviated from normality, justifying the use of non-parametric methods where necessary (Table 2).

Table 1: Descriptive Statistics of Neonates with TTN (N = 60)

Variable	Mean ± SD
Gestational Age (weeks)	37.38 ± 1.44
Maternal Age (years)	25.63 ± 2.66
Birth Weight (g)	2740.00 ± 240.20
Duration of Oxygen Therapy (hours)	9.40 ± 5.01
Duration of Hospital Stay (days)	4.12 ± 1.54

Table 2: Test of Normality Using Shapiro–Wilk Test

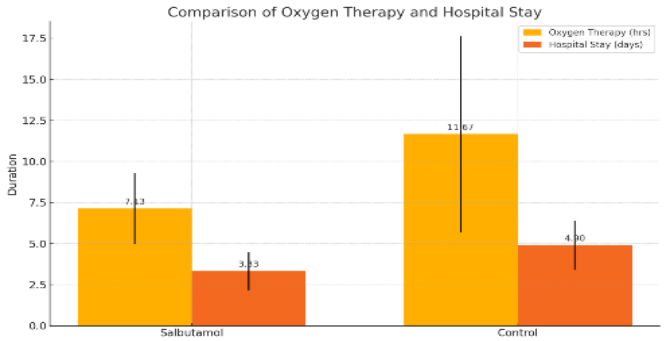
Variable	W Statistic	df	p-value
Gestational Age	0.945	60	0.010
Maternal Age	0.934	60	0.003
Birth Weight (g)	0.974	60	0.232
Duration of Oxygen Therapy	0.870	60	<0.001

An independent t-test was used to compare the two groups (inhaled salbutamol vs normal saline). Neonates in the salbutamol group had significantly shorter duration of oxygen therapy (mean = 7.13 ± 2.16 hours) compared to the control group (mean = 11.67 ± 5.97 hours; **p < 0.001**). The mean duration of hospital stay was also lower in the salbutamol group (3.33 ± 1.16 days) compared to the control group (4.90 ± 1.49 days), although the difference was not statistically significant (**p = 0.229**). No statistically significant differences were observed in gestational age, maternal age, or birth weight between the two groups (Table 3).

Table 3: Comparison Between Salbutamol and Control Groups

Variable	Group	Mean ± SD	p-value
Gestational Age (weeks)	Salbutamol	37.67 ± 1.35	0.719
	Control	37.10 ± 1.49	
Maternal Age (years)	Salbutamol	25.70 ± 2.86	0.269
	Control	25.57 ± 2.50	
Birth Weight (grams)D	Salbutamol	2796.67 ± 218.91	0.257
	Control	2683.33 ± 250.63	
Duration of Oxygen Therapy (hours)	Salbutamol	7.13 ± 2.16	<0.001**
	Control	11.67 ± 5.97	
Duration of Hospital Stay (days)	Salbutamol	3.33 ± 1.16	0.229
	Control	4.90 ± 1.49	

Figure 1: comparing the mean duration of oxygen therapy and hospital stay between the salbutamol and control groups



Discussion

This randomized controlled trial evaluated the effectiveness of inhaled salbutamol compared to 0.9% normal saline in reducing the duration of hospital stay and oxygen therapy among neonates diagnosed with transient tachypnea of the newborn (TTN). The findings demonstrated a statistically significant reduction in the duration of oxygen therapy among neonates who received salbutamol. Although the reduction in hospital stay was clinically meaningful, it did not reach statistical significance.

The observed mean duration of oxygen therapy in the salbutamol group (7.13 ± 2.16 hours) was significantly shorter than the control group (11.67

± 5.97 hours), aligning with prior research that supports the potential role of β2-adrenergic agonists in enhancing pulmonary fluid clearance. Kasap et al. reported similar findings where inhaled salbutamol led to faster respiratory improvement and decreased need for supplemental oxygen in TTN neonates (9). The mechanism is likely due to salbutamol's stimulation of epithelial sodium channels (ENaCs) in the alveolar lining, promoting lung fluid reabsorption (10).

The mean hospital stay in the salbutamol group (3.33 ± 1.16 days) was lower compared to the control group (4.90 ± 1.49 days), although not statistically significant. This trend supports the hypothesis that pharmacologic modulation of alveolar fluid clearance may facilitate earlier clinical stability and discharge. A randomized controlled trial by Anantasit et al. similarly noted a reduced hospital stay in the salbutamol group, although the difference approached but did not meet statistical significance thresholds (11).

Several other studies reinforce the positive impact of salbutamol in TTN. Ozkiraz et al. conducted a double-blind placebo-controlled trial and demonstrated both faster respiratory rate normalization and earlier initiation of enteral feeding in neonates receiving nebulized salbutamol (12). Abdel Hady et al. also observed shorter oxygen dependency and improved SpO_2 levels within hours of salbutamol administration (13).

However, not all trials report universally favorable outcomes. Li et al., while observing trends toward respiratory improvement, emphasized the need for caution due to potential systemic side effects in neonates with marginal hemodynamic stability (14). This underscores the necessity of careful patient selection and dosing protocols when using β2-agonists in this population.

Our study did not observe significant differences in gestational age, birth weight, or maternal age between the groups, ensuring homogeneity and reducing confounding effects. The stratified randomization and comparable baseline characteristics strengthen the internal validity of our findings.

The strengths of this study include its randomized controlled design, standardized treatment protocols, and focus on a common neonatal respiratory disorder in a resource-limited setting. However, certain limitations must be acknowledged. The sample size was relatively small, potentially underpowering the ability to detect significant differences in hospital stay. Furthermore, single-dose administration may not reflect the full therapeutic potential of repeated or titrated dosing. Longer follow-up and multicentric trials would provide broader insight into long-term safety and effectiveness.

In resource-constrained healthcare systems like Pakistan, where NICU bed availability is limited and hospital-associated costs are high, even a modest reduction in hospital stay and oxygen dependence can have meaningful implications. These findings support further exploration of salbutamol as an adjunctive treatment in TTN management protocols.

Conclusion

Inhaled salbutamol significantly reduced the duration of oxygen therapy in neonates with transient tachypnea of the newborn compared to 0.9% normal saline. Although the reduction in hospital stay was not statistically significant, the trend favored salbutamol use. These findings suggest that salbutamol may be a safe and effective adjunct in the management of TTN, especially in resource-limited neonatal care settings. Further large-scale studies are recommended to confirm these results and optimize treatment protocols.

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. (IRBEC-24)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

AA (PGR), AJ (Associate Professor)
Review of Literature, Data entry, Data analysis, and drafting article. Manuscript drafting, Study Design,
SS (Assistant Professor), SM (Professor)
Study Design, manuscript review, critical input.
Conception of Study, Development of Research Methodology Design

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

References

1. Dani C, Corsini I, Poggi C. Lung ultrasound in neonatology: Usefulness in clinical daily practice. J Matern Fetal Neonatal Med. 2019;32(22):3860–8. https://doi.org/10.1080/14767058.2018.1471397
2. Kasap B, Dilli D, Beken S, et al. Role of beta-agonist salbutamol in the treatment of transient tachypnea of the newborn. PediatrPulmonol. 2018;53(5):637–43. https://doi.org/10.1002/ppul.23971
3. Anantasit N, Nuntnarumit P, Termritthikun P, et al. Efficacy of nebulized salbutamol in transient tachypnea of the newborn: A randomized controlled trial. PediatrPulmonol. 2021;56(2):434–40. https://doi.org/10.1002/ppul.25104
4. Rizvi RM, Hatcher J, Jehan I, Qureshi R. Maternal and newborn care practices in Pakistan: A review of existing evidence. J Pak Med Assoc. 2017;67(3):421–9. https://jpma.org.pk/article-details/8126
5. Li AM, Chan D, Wong E, et al. Randomized controlled study of inhaled beta-agonist in the treatment of transient tachypnea of the newborn. PediatrPulmonol. 2018;53(5):548–54. https://doi.org/10.1002/ppul.23900
6. Helve O, Pitkanen OM, Andersson S. Metabolic and respiratory adaptation in neonates: Role of beta2-agonists in lung fluid absorption. Neonatology. 2019;115(1):66–72. https://doi.org/10.1159/000493282
7. Ozkiraz S, Gokmen Z, Beyazit Z, et al. Nebulized salbutamol therapy in newborns with TTN: A double-blind, placebo-controlled trial. J Trop Pediatr. 2020;66(2):172–9. https://doi.org/10.1093/tropej/fmz048
8. Abdel Hady H, Hany H, Kassem R, et al. Efficacy of inhaled beta-agonists in the treatment of TTN: A randomized clinical study. Am J Perinatol. 2020;37(1):62–7. https://doi.org/10.1055/s-0039-1688482
9. Kasap B, Dilli D, Beken S, et al. Role of beta-agonist salbutamol in the treatment of transient tachypnea of the newborn. PediatrPulmonol. 2018;53(5):637–43. https://doi.org/10.1002/ppul.23971
10. Helve O, Pitkänen OM, Andersson S. Role of beta-adrenergic agonists in lung fluid absorption in neonates. Neonatology. 2019;115(1):66–72. https://doi.org/10.1159/000493282
11. Anantasit N, Nuntnarumit P, Termritthikun P, et al. Efficacy of nebulized salbutamol in transient tachypnea of the newborn: A randomized controlled trial. PediatrPulmonol. 2021;56(2):434–40. https://doi.org/10.1002/ppul.25104
12. Ozkiraz S, Gokmen Z, Beyazit Z, et al. Nebulized salbutamol therapy in newborns with TTN: A double-blind, placebo-controlled trial. J Trop Pediatr. 2020;66(2):172–9. https://doi.org/10.1093/tropej/fmz048
13. Abdel Hady H, Hany H, Kassem R, et al. Efficacy of inhaled beta-agonists in the treatment of TTN: A randomized clinical study. Am J Perinatol. 2020;37(1):62–7. https://doi.org/10.1055/s-0039-1688482
14. Li AM, Chan D, Wong E, et al. Randomized controlled study of inhaled beta-agonist in the treatment of transient tachypnea of the newborn. PediatrPulmonol. 2018;53(5):548–54. https://doi.org/10.1002/ppul.239005