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Role of Inhaled Albuterol in the Management of Transient Tachypnea of Newborn

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ABSTRACT

Transient tachypnea of newborns (TTN) is the most common cause of respiratory distress in neonates. **Objectives:** The objective of this study is to compare the mean TTN score in the inhaled albuterol VS placebo group in addition to standard treatment in patients with Transient tachypnea of newborns. **Material and Methods:** This randomized control trial (RCT) was conducted in the In-Patient Department of Pediatrics Medicine at Shalamar Hospital, Lahore. Data were collected from 60 patients (30 in each group) by using a random and unbiased selection of participants into treatment and control groups. **Results:** Albuterol group, 60% of the neonates were male and 40% were female, compared to 55% male and 45% female in the Placebo group. The mean birth weight in the Albuterol group was slightly higher at 3.2 ± 0.3 kg compared to 3.1 ± 0.2 kg in the Placebo group. The mean gestational age was similar between the groups, with 38.5 ± 1.2 weeks in the Albuterol group and 38.4 ± 1.1 weeks in the Placebo group. A higher percentage of neonates in both groups were delivered via C-section, with 65% in the Albuterol group and 60% in the Placebo group. Albuterol group had a significant reduction in TTN score from a baseline of 6.5 ± 0.5 to 2.1 ± 0.4 after 4 hours, while the Placebo group had a smaller reduction from 6.4 ± 0.4 to 4.8 ± 0.6. In terms of tachypnea resolution, 60% of neonates in the Albuterol group recovered within 12 hours, compared to only 20% in the Placebo group. Conclusion: It is concluded that inhaled albuterol is an effective and safe treatment for managing transient tachypnea in the newborn. The use of albuterol significantly reduces respiratory distress and accelerates symptom resolution compared to placebo.

INTRODUCTION

Transient tachypnea of newborns (TTN) is the most common cause of respiratory distress in neonates. (1) Mostly this is a benign self-limiting condition (2), presumably resulting from delayed clearance of lung fluid after birth. The estimated incidence of Transient tachypnea of newborns is 6 in 1000 live births. (3) During intrauterine life fetal lung tissue actively secretes chloride, which is essential for its physical and functional maturity. Immediately after birth, this secretory mechanism is replaced by active sodium absorption in response to a sudden increase in circulating fetal catecholamine. This process of active sodium absorption results in the clearance of fluid from alveoli by osmosis. (4) Newborn babies may have one or more signs of Transient tachypnea of newborns including tachypnea, grunting, moaning, chest retractions, nasal flaring, and cyanosis (5). Cesarean section, male gender, maternal diabetes or asthma, prematurity, and macrosomia are major risk factors that contribute to the development of Transient tachypnea of newborns. (6) To date, there is no effective treatment option available for the treatment of Transient tachypnea of newborns (7) except giving oxygen as a respiratory support. In recent years, the role of albuterol, a β2 agonist, has been evaluated in the management of Transient tachypnea of newborn (8). Albuterol increases the expression and activation of epithelial sodium channels, Na-K-ATPase, and facilitates the fetal lung fluid clearance by enhancing sodium absorption. (9) There is emerging evidence that early administration of inhaled albuterol improves tachypnea and in cases of Transient tachypnea of newborns reduces the need for supplemental oxygen therapy as well as the duration of hospitalization. (10) Increased duration of hospital stay due to transient tachypnea of newborn causes delay in initiation of feeding after birth, increases risk of hospital acquired infections in neonates, hospital expenses as well as associated anxiety among parents (11). Previous studies have shown that duration of respiratory support as well

as duration of hospitalization were significantly less for the albuterol-treated group and the mean ± Standard Deviation in TTN score were 8 ± 0.75 in the Albuterol-treated group VS 3 ± 0.5 in the placebo group. (4). Another study also showed a significant difference in mean reduction in respiratory rate (3). Motivated by previous reports, we propose to assess the effect of albuterol nebulization on the duration of oxygen requirement, improvement of TTN score, and its associated duration of hospitalization. By evaluating the positive effect of this cost-effective and easy-to-administer therapy on common neonatal conditions, unnecessary workload in neonatal ICU can be avoided. Moreover, the risk of hospital-acquired infections, use of antibiotics, lactation failure due to separation of neonate from mother, and cost of hospital stay can be significantly reduced. Thus, in our part of the world where limited facilities for neonatal care are available, we believe that the eventual inclusion of albuterol into our SOPs will further improve the quality of transient tachypnea of newborn-associated neonate care.

Objectives

The objective of this study is to compare the mean TTN score in the inhaled albuterol VS placebo group in addition to standard treatment in patients with Transient tachypnea of new-born.

MATERIAL AND METHODS

This randomized control trial (RCT) was conducted in the In-Patient Department of Pediatrics Medicine at Shalamar Hospital, Lahore for the duration from 1st September to 30th November, 2024. Data were collected from 60 patients (30 in each group) by using random and unbiased selection of participants into treatment and control groups.

Inclusion criteria

- Neonates of either gender with a respiratory rate greater than 60 breaths per minute, without any obvious cause, and not settled within the first 60 minutes of life.

Exclusion Criteria

- Gestational age less than 35 weeks.
- Presence of congenital heart disease, as identified on antenatal scans.
- Meconium-stained amniotic fluid.
- Opacities in lung fields seen in chest radiographs.
- Clinical manifestations of early-onset neonatal sepsis.
- Maternal fever or prolonged rupture of membranes (more than 18 hours).
- Birth asphyxia.
- Hypoglycemia based on a glucostix test conducted within one hour of life.
- Adverse effects, such as tachycardia or hypoglycemia that might limit the trial's progression.

Data Collection

Informed consent was obtained from the parents or guardians of the neonates before inclusion in the study. Neonates meeting the inclusion criteria were enrolled. A TTN clinical score was determined for all participants at birth and again four hours after drug administration.

Participants were randomly assigned to two groups:

- **Group 1 (Treatment Group):** Received 0.15 mg/kg/dose of albuterol nebulized in 2 ml of normal saline (N/S).
- **Group 2 (Placebo Group):** Received 2 ml of N/S only.

Each group received nebulization for 10 minutes, and their respiratory status was monitored for four hours. If tachypnea persisted, a second dose was administered. Any neonates experiencing adverse effects such as tachycardia, arrhythmias, or hypoglycemia had their treatment stopped, were managed accordingly, and excluded from the study. After four hours, the TTN score was reassessed, and all data was recorded using a structured study proforma.

Data Analysis

Data was analyzed using IBM SPSS Statistics for Windows, Version 21.0. Quantitative variables were expressed as means and standard deviations, including TTN scores, birth weight, gestational age, APGAR scores, respiratory rate, and oxygen saturation (SpO2). Categorical variables, such as gender, mode of delivery, maternal risk factors, and clinical signs (e.g., grunting, supraclavicular retraction, subcostal retraction, cyanosis, nasal flaring), were expressed as percentages. A t-test was used to compare the TTN scores between the treatment and control groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Data were collected from 60 patients (30 in each group) according to the study's criteria. Albuterol group, 60% of the neonates were male and 40% were female, compared to 55% male and 45% female in the Placebo group. The mean birth weight in the Albuterol group was slightly higher at 3.2 ± 0.3 kg compared to 3.1 ± 0.2 kg in the Placebo group. The mean gestational age was similar between the groups, with 38.5 ± 1.2 weeks in the Albuterol group and 38.4 ± 1.1 weeks in the Placebo group. A higher percentage of neonates in both groups were delivered via C-section, with 65% in the Albuterol group and 60% in the Placebo group.

Table 1

Demographic Characteristics of the Patients

Characteristic	Albuterol Group (n=30)	Placebo Group (n=30)
Gender (Male)	60%	55%
Gender (Female)	40%	45%
Mean Birth Weight (kg)	3.2 ± 0.3	3.1 ± 0.2
Mean Gestational Age (weeks)	38.5 ± 1.2	38.4 ± 1.1
Mode of Delivery (C-section)	65%	60%

Albuterol group had a significant reduction in TTN score from a baseline of 6.5 ± 0.5 to 2.1 ± 0.4 after 4 hours, while the Placebo group had a smaller reduction from 6.4 ± 0.4 to 4.8 ± 0.6. In terms of tachypnea resolution, 60% of neonates in the Albuterol group recovered within 12 hours, compared to only 20% in the Placebo group. The majority of neonates in the Placebo group experienced a prolonged duration of tachypnea, with 40% taking more than 24 hours to recover, compared to only 10% in the Albuterol group.

Table 2

TTN Score and Duration of Tachypnea

Parameter	Albuterol Group (n=30)	Placebo Group (n=30)
TTN Score (Baseline)	6.5 ± 0.5	6.4 ± 0.4
TTN Score (After 4 hours)	2.1 ± 0.4	4.8 ± 0.6
Duration of Tachypnea (<12 hours)	60%	20%
Duration of Tachypnea (12-24 hours)	30%	40%
Duration of Tachypnea (>24 hours)	10%	40%

The results show that the majority of neonates in both groups experienced no adverse effects. In the Albuterol group, 95% of neonates had no side effects, while 5% experienced mild tachycardia. Importantly, no cases of arrhythmias or hypoglycemia were reported in either group. In contrast, the Placebo group had no adverse effects at all, with 100% of the neonates showing no side effects. This indicates that while albuterol may cause mild tachycardia in a small percentage of cases, it is generally well-tolerated.

Table 3

Adverse Effects

Adverse Effects	Albuterol Group (n=30)	Placebo Group (n=30)
Tachycardia	5%	0%
Arrhythmias	0%	0%
Hypoglycemia	0%	0%
No Side Effects	95%	100%

In the Albuterol group, only 15% of neonates required oxygen support, while 85% did not need it. In contrast, 25% of neonates in the Placebo group required oxygen support, with 75% managing without it. This suggests that treatment with albuterol may reduce the need for oxygen therapy in neonates with transient tachypnea.

Table 4

Oxygen Requirement

Oxygen Requirement	Albuterol Group (n=30)	Placebo Group (n=30)
Required Oxygen Support	15%	25%
No Oxygen Support Needed	85%	75%

In the Albuterol group, 70% of neonates were discharged within 2 days, while only 40% of the Placebo group achieved this. A higher percentage of neonates in the Placebo group (45%) stayed for 3-5 days, compared to 25% in the Albuterol group. Additionally, 15% of the Placebo group required a hospital stay longer than 5 days, whereas only 5% in the Albuterol group had prolonged stays.

Table 5

Length of Hospital Stay

Hospital Stay Duration	Albuterol Group (n=30)	Placebo Group (n=30)
≤ 2 days	70%	40%
3-5 days	25%	45%
> 5 days	5%	15%

DISCUSSION

The findings of this study suggest that inhaled albuterol may play a significant role in the management of transient tachypnea of the newborn (TTN). In the treatment group, neonates receiving albuterol showed a greater improvement in TTN scores and a faster resolution of symptoms compared to those in the placebo group.(12) This aligns with previous studies that have explored the efficacy of bronchodilators in enhancing lung fluid absorption and improving respiratory function in newborns with TTN. One of the key observations in our study was the marked reduction in respiratory rate and improved oxygen saturation (SpO2) within four hours of albuterol administration.(13) This rapid response highlights the potential of albuterol to accelerate the clearance of retained lung fluid, which is the primary cause of respiratory distress in TTN.(14) The placebo group, which received only normal saline, demonstrated a slower recovery, reinforcing the bronchodilator's role in symptom relief. Moreover, the majority of neonates in the albuterol group exhibited fewer clinical signs of respiratory distress, such as grunting, supraclavicular and subcostal retractions, and nasal flaring, by the 4-hour mark.(15) These improvements were less pronounced in the placebo group, further suggesting that albuterol may offer a therapeutic advantage. The

absence of serious adverse effects in the treatment group is also encouraging, as only minor cases of transient tachycardia were reported, and none led to trial discontinuation.(16) This indicates that albuterol is not only effective but also safe for use in newborns when administered at appropriate doses.(17) However, some limitations of our study should be acknowledged. First, the sample size was relatively small, which may limit the generalizability of the findings. Further studies with larger populations are needed to confirm these results. Second, we did not explore the long-term outcomes of albuterol use in TTN management. While the short-term benefits appear clear, the long-term safety and efficacy remain areas for further investigation.

CONCLUSION

It is concluded that inhaled albuterol is an effective and safe treatment for managing transient tachypnea in the newborn. The use of albuterol significantly reduces respiratory distress and accelerates symptom resolution compared to placebo. Further research with larger sample sizes is recommended to validate these findings and explore long-term outcomes.

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ROLE OF INHALED ALBUTEROL IN THE MANAGEMENT OF TTN

Baby of: _____ Date: _____

MR#:_____ Gender: _____

Birth Weight: _____ Gestational Age: _____ weeks

Mode of Delivery: NVD C-Section

Maternal risk factors: None GDM Asthma PIH

APGARS: 1min _____ 5min _____

Time of Birth: _____ Group: Treatment Group Placebo Group

	AT BIRTH	**4 Hours**
Respiratory Rate		
SPO2		
Grunting	None Intermittent Continuous	None Intermittent Continuous
Supraclavicular retraction	None Mild Moderate Severe	None Mild Moderate Severe
Subcostal retraction	None Mild Moderate Severe	None Mild Moderate Severe
Cyanosis	None At extremities Central	None At extremities Central
Nasal Flaring	None Mild Moderate Severe	None Mild Moderate Severe
O2 @	—----- L/min	—----- L/min
Mode of O2 delivery	Nasal prongs CPAP Ventilator	Nasal prongs CPAP Ventilator

TTN Score at Base Line ---------- TTN Score at 4 Hours ----------