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# Comparison of Effects of Inhaled Salbutamol with Placebo in Management of Transient Tachypnea of Newborn

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## ABSTRACT

***Objective:*** To compare the outcome of inhaled Salbutamol (Albuterol) with normal saline (Placebo) in terms of mean duration of oxygen therapy and mean hospital stay in newborns with transient tachypnea of the newborn.

***Study Design:*** Quasi-experimental study.

***Place and Duration of Study:*** Department of Paediatrics, Islamic International Medical College, Trust Pakistan Railway General Hospital, Rawalpindi Pakistan, from Jan to Dec 2019.

***Methodology:*** One hundred newborns meeting the inclusion criteria were enrolled. All newborns included in this study had X-ray chests. Neonates were divided into Groups A and B by lottery method. Group-A received inhaled Salbutamol plus 2 ml normal saline 0.9% by nebulizer, and Group-B received 0.9% normal saline by nebulizer six hourly and outcomes were recorded.

***Results:*** In this study, 32(32%) patients were female newborns, and 68(68%) were male babies. 97(97%) babies were delivered by Caesarean section. In Salbutamol-Group, the mean duration of oxygen inhalation was 20.86±10.79 hours, while in Placebo-Group, the mean was 40.42±16.64 hours ($p$-value<0.05). Similarly, in the Salbutamol-Group the mean hospital duration was 46.70±31.93 hours, while in the Placebo- Group, the mean was 74.08±54.76 hours ($p$-value<0.05)

***Conclusion:*** This study concluded that Salbutamol inhalation significantly reduces the need for oxygen and hospital stay compared with Placebo in newborns with Transient Tachypnea of the newborn.

**Keywords:** Hospital Stay, Oxygen Inhalation, Salbutamol, Transient tachypnea of the newborn.

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## INTRODUCTION

Transient tachypnea of newborn (TTN) is characterized by tachypnea and signs of respiratory distress. It is the respiratory disorder of term and late preterm neonates secondary to delayed or impaired clearance mechanism of retained fetal lung fluids after birth.[1,2] It is among the common causes of respiratory distress in late preterm and term babies, with an overall incidence of 4-6% of live births.[3] Clinical findings in these neonates are signs of respiratory distress like tachypnea, expiratory grunting, nasal flaring, and subcostal/ intercostal recession at or soon after birth.[4] X-ray shows fluid in the horizontal fissure, and ultrasound shows double lung points.[5] Treatment of TTN is supportive, including O2 supplementation, with holding enteral feeding and IV fluids. Nevertheless, oxygen administration and admission to the nursery pose a significant financial burden on families and hospital resources.[6] Severe hypoxia and death can develop in some neonates, constituting the "malignant TTN" entity. It is associated with wheezing syndrome in late childhood.[7,8]

Therefore, there is a need to search for treatment options that could prevent or reduce the risk of complications, the need for oxygen supplementation and shorten the hospital stay.[9] A shorter stay in the hospital and reduced oxygen requirement mitigate the risk of acquiring nosocomial infections in neonates. It eases the workload on already burdened Neonatal Intensive Care Units in our country.

Many studies have been conducted over the last two decades comparing inhaled/ oral/ injectable furosemide, inhaled steroids and beta-adrenergic agents. The results, however, are variable.[9,10]

We intend to conduct this study to determine the possible benefits of inhaled Salbutamol in TTN. Inhaled Salbutamol is simple to administer and cost-effective, and if found effective, it could reduce the burden on families' hospital resources and improve outcomes in a country like Pakistan.

## METHODOLOGY

The quasi-experimental study was conducted at the Department of Paediatrics of Islamic International Medical College Trust Pakistan Railway General

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Hospital, Rawalpindi Pakistan, from January to December 2019. The sample size was calculated by World Health Organization (WHO) calculator with population mean oxygen therapy duration in hours in Salbutamol Group=17.12, population mean oxygen therapy duration in hours in control Group=32.72, population standard deviation=22.55.[11] Non-proba-bility consecutive sampling technique was used.

**Inclusion Criteria:** Patients of either gender with gestational age 34 weeks or more from birth to 3 days of life with clinical or radiological evidence of TTN were included in the study.

**Exclusion Criteria:** Newborns with a history of meconium aspiration, birth asphyxia, pneumonia, RDS, congenital heart disease and congenital anomalies were excluded from the study.

After approval from the Hospital Ethical Committee, 100 newborns meeting the inclusion criteria were included in the study from the pediatric Department of IIMC Railway General Hospital neonatal intensive care unit. After obtaining informed consent from the parents, demographic details (Name, age, sex, gestational age and birth weight), maternal risk factors (gestational diabetes, chorioamnionitis and maternal asthma) and birth history (mode of delivery, meconium Staining and delayed crying after birth) were also obtained. All newborns included in this study had X-ray chests.

Neonates were randomly divided into groups A and B by lottery methods. Group-A received 0.15ml /kg (equal to 0.15mg/kg) inhaled Salbutamol (Ventolinsoln. GSK) with 2 ml normal saline 0.9% by nebulizer, and Group-B (or Placebo) received 0.9% normal saline by nebulizer six hourly. Blood samples were collected for blood culture sensitivity, complete blood count, and C-reactive protein at admission. All neonates were kept nil per oral till tachypnea and respiratory distress resolved. Intravenous fluids were administrated at 60ml/kg/day on day 1 for full term and 80ml/kg/day for preterm.

The respiratory rate oxygen saturation was monitored every two hours till discharge. Major study outcomes like duration of oxygen therapy, time to initiation of oral feeding and length of hospital stay were recorded for each patient.

Data was analyzed using the SPSS vers 21. Mean± SD was calculated for quantitative variables. Frequency and percentage were calculated for categorical variables. Chi-square test and Independent sample t-test were used. The *p*-value of 0.05 or less was taken as significant.

## RESULTS

Our study included 100 newborn patients, fulfilling the inclusion criteria. Among them, there were 68(68%) male and 32(32%) were females. In the Salbutamol Group, the mean gestational age of the patients was 36.92±1.39 weeks, while in the Placebo Group, the mean gestational age of the patients was 36.08±1.08 weeks.

In the Salbutamol Group, at the 48$^{th}$ hour, the mean respiratory rate of the patients was 53.06±10.822, while in the Placebo Group, the mean respiratory rate was 57.48±9.704 (*p*-value=0.034). In the Salbutamol Group, the mean duration of oxygen inhalation was 20.86±10.79 hours, while in the placebo Group, the mean was 40.42±16.64 hours (*p*-value<0.05) Table-I. Similarly, in the Salbutamol Group, the mean hospital duration was 46.70±31.93 hours, while in the Placebo Group, the mean was 74.08±54.76 hours (*p*-value<0.05), as shown in Table-II.

**Table-I: Comparison of Oxygen Inhalation Duration (hours) between study Groups (n=100)**

| Study Groups | | *p*- value |
|---|---|---|
| Salbutamol Group(n=50) | Placebo Group(n=50) | |
| 20.86±10.79 hours | 40.42±16.64 hours | < 0.001 |

**Table-II: Comparison of hospital duration (hours) between study Groups (n=100)**

| Study Group | | *p*-value |
|---|---|---|
| Salbutamol Group(n=50) | Placebo Group(n=50) | |
| 46.70±31.93 hours | 74.08±54.76 hours | 0.003 |

Furthermore, a significant difference was found between the study Groups and oxygen inhalation of the patients according to gestational age, gender, birth weight and mode of delivery (*p*-value<0.05) (Table-III).

**Table-III: Comparison of Oxygen Inhalation between study Groups according to Gestational Age, Gender, Birth Weight & Mode of Delivery (n=100)**

| Oxygen inhalation | Study Groups | n | Mean±SD | *p*-value |
|---|---|---|---|---|
| **Mode of delivery** | | | | |
| ≤37 | Salbutamol | 33 | 22.21±11.14 | <0.001 |
| | Placebo | 27 | 37.56±16.95 | |
| >37 | Salbutamol | 17 | 18.24±9.88 | <0.001 |
| | Placebo | 23 | 43.78±15.99 | |
| **Gender** | | | | |
| Male | Salbutamol | 33 | 19.67±11.12 | <0.001 |
| | Placebo | 35 | 42.83±14.82 | |
| Female | Salbutamol | 17 | 23.18±10.04 | 0.040 |
| | Placebo | 15 | 34.80±19.68 | |
| **Birth Weight (grams)** | | | | |
| ≤3000 | Salbutamol | 29 | 21.31±10.79 | 0.015 |
| | Placebo | 13 | 38.54±21.28 | |
| >3000 | Salbutamol | 21 | 20.24±11.02 | <0.001 |
| | Placebo | 37 | 41.08±14.98 | |
| **Mode of Delivery** | | | | |
| SVD | Salbutamol | 1 | 24.00 ±000 | -- |
| | Placebo | 2 | 48.00±000 | |
| CS | Salbutamol | 49 | 20.80±10.895 | <0.001 |
| | Placebo | 48 | 40.10±16.918 | |

## DISCUSSION

This study observed significant differences between patients given Salbutamol vs. Placebo. The rationale for using Salbutamol for transient tachypnea of the newborn is based on studies concluding that β-agonists can accelerate the rate of clearance of fluid from alveoli. In our study, Salbutamol inhalation reduced patients' mean duration of oxygen requirement and the mean length of stay in the hospital (*p*-value<0.001). Mohammadzadeh *et al*.[12] concluded that Salbutamol decreased the duration of supplemental oxygen therapy (p=0.04) and overall hospital stay (*p*=0.006) as well as the commencement of oral feeds (*p*=0.013) in comparison to those in the placebo Group. In a similar study, Armangil *et al*. revealed the effectiveness of a single dose of inhaled beta-2 agonist (Salbutamol) treatment in terms of clinical and laboratory findings without any untoward effects.[13]

A study by Moresco *et al*.[14] documented in their study findings that the duration of supplemental oxygen therapy in newborns is decreased in newborns with transient tachypnea who are treated with Salbutamol. In another study by Mussavi *et al*.[10] continuous positive airway pressure duration was significantly less in the infants treated with Albuterol 1.6±0.77 vs Placebo 3.3±0.98 (*p*-value 0.0001). Buchiboyina *et al*.[15] found a remarkable difference between the Salbutamol and placebo Groups in terms of treatment duration, hospitalization, need for supplemental oxygen (continuous positive airway pressure), and initiation of enteral feeding. Moreover, they did not observe any adverse effects of treatment. Another study in Korea by Kim *et al*. revealed that patients who receive Salbutamol have a noteworthy lesser duration of supplemental oxygen therapy and a reduced number of days of empiric antibiotic therapy.[16] TTN is among the common causes of respiratory distress in late preterm and term babies. It may sometimes be a self-limited condition, but in other cases, some therapies may be required for its management. TTN is diagnosed clinically, but in some cases, radiological investigations may be carried out to rule out other serious conditions.[17,18]

## CONCLUSION

Salbutamol (Albuterol) inhalation significantly reduces the need for oxygen and hospital stay compared with Placebo in newborns with TTN. In a country like Pakistan, with limited Healthcare facilities and a lower per capita income, using Salbutamol in neonates with TTN reduces the financial burden and stress on their parents and eludes undue burden on Healthcare facilities.

**Conflict of Interest:** None.

**Author's Contribution**

Following authors have made substantial contributions to the manuscript as under:

KR: & FAS: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

SAS: & BA: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AA & SAS: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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