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Effect of salbutamol nebulization in transient tachypnea of newborn

***Amanpreet Kaur, **Pardeep Singh Kahlon, ***Karnail Singh, ***MS Pannu**

*Junior Resident, **Assistant Professor, ***Professor, Department of Paediatrics, Govt. Medical College, Amritsar, India, 143001

Corresponding Author: **Dr. Pardeep Singh Kahlon**, Assistant Professor, Department of Paediatrics, Govt. Medical College, Amritsar, India, 143001

E- mail:docpsk@yahoo.com

Abstract

Background: Transient tachypnea of newborn (TTN) is a parenchymal lung disease present in neonates usually within 6 hours of life. Signs of TTN usually persist for 12-24 hours in mild disease but can last up to 72 hours in more severe cases. In severe cases of TTN, complications such as pneumothorax, need for extracorporeal membrane oxygenation, and death have been reported.

Objective: To study the effect of single dose of salbutamol nebulization in TTN administered at diagnosis and assess its efficacy at 30 minutes, 1 hour and 4 hours post nebulization and the side effects if any at 4 hours

Materials and methods:

Study design: Double blind prospective placebo controlled study, one dose of inhaled salbutamol or normal saline solution was administered to 50 newborns each with gestational age of 35 to 41 weeks and diagnosed as TTN according to clinical and radiological features. **Setting:** Pediatrics Department, Bebe Nanki Mother and Child Care Centre, Government Medical College, Amritsar. **Participants:** 100 newborns. **Outcome variables:** TTN score, oxygen saturation, respiratory rate and average duration of hospital stay.

Results: After one dose of salbutamol nebulization, the TTN score, respiratory rate, oxygen saturation and duration of hospitalization did not decrease significantly when compared with the normal saline group (p value >0.05). No side effects like tachycardia, hypokalemia and hyperglycemia were noted in salbutamol group when compared to normal saline group.

Conclusion: Inhaled salbutamol treatment did not show any effect on early resolution of symptoms and early discharge of babies.

Keywords: TTN, Salbutamol nebulization.

Introduction

Transient tachypnea of newborn (TTN) is parenchymal lung disease. It is the benign self-limited condition resulting from delayed resorption of foetal lung fluid¹. This condition is characterised by:-

- Tachypnea with signs of mild respiratory distress including retractions, grunting, nasal flaring and mild cyanosis.
- Decreased oxygen saturation alleviated by supplemental oxygen with FiO_2 less than 40%².

It is the common cause of respiratory distress in the immediate new born period. In a review of 33,289 term deliveries (37 to 42 weeks), the incidence of TTN was 5.7 per 1000 births³.

Infants with TTN present within the first 6 hours of life. Signs of TTN usually persist for 12-24 hours in mild disease but can last up to 72 hours in more severe cases². Although it is self limited condition, there is an increase data to suggest that TTN increases risk for developing a wheezing syndrome early in the life⁴. During late gestation, in response to increased concentrations of catecholamines and other hormones, the mature lung epithelium switches from actively secreting chloride and liquid into the air spaces to actively reabsorbing sodium and liquid⁵⁻⁶. Increased oxygen tension at birth enhances the capacity of the epithelium to transport sodium and increases gene expression of the epithelial sodium channel (ENaC) followed by transport into the interstitium via basolateral Na^+/K^+ -ATPase and passive movement of chloride and water through the paracellular and intracellular pathways⁶. Epithelial sodium channels play a crucial role in lung liquid clearance at birth. In fact, the first evidence of involvement of these receptors came from measurements of an amiloride-induced drop in potential difference between the nasal epithelium and subcutaneous space in newborns. Gowen et al⁷ demonstrated that this potential difference was reduced in infants with TTN (suggesting a defect in sodium trans- port), and recovery from TTN in 1 to 3 days was associated with an increase in potential difference to normal level. Passive resorption of liquid also occurs after birth because

of differences among the oncotic pressure of air spaces, interstitium, and blood vessels. The majority of water transport across the apical membrane is thought to occur through aquaporin 5 (AQP5) water channels⁸.

Materials and Methods

This prospective study was conducted on 100 newborns diagnosed with TTN admitted in the Paediatrics Department of Bebe Nanki Mother and Child Care Centre attached to Government Medical College and Hospital, Amritsar. The study criteria of patients are described as follows-

Selection of cases

Inclusion criteria

1. Neonates (35 to 41 weeks of gestation) diagnosed as TTN (according to Rawling and Smith Criteria)

Exclusion criteria

1. Premature neonates [<35 weeks]
2. Neonates requiring respiratory support in form of CPAP and mechanical ventilation.
3. Exclusion of other known respiratory disorders like:
 - Meconium Aspiration- irregular pattern of increased density throughout lung, no meconium staining of skin
 - Respiratory Distress Syndrome- having reticulo-granular pattern in x-rays picture, premature neonates, no surfactant therapy.
 - Congenital heart disease-having murmur, signs of heart failure.
 - Birth asphyxia-history suggestive of intrauterine asphyxia, delayed cry at birth.

TTN was diagnosed according to Rawlings and smith⁹ which is based on the radiologic and clinical findings-

- 1] Early(within 6 hours of birth) onset of tachypnea [in uneventful late preterm(35-36weeks)or term newborn]

2] Persistence of tachypnea sometimes with retractions, or expiratory grunting and, occasionally, cyanosis that is relieved by minimal oxygen supplementation.

3] Chest generally sounds clear without rales or rhonchi.

Chest radiograph shows:

- Prominent pulmonary vascular markings.
- Fluid in the interlobar fissure.
- Flat diaphragms and rarely pleural effusion.
- Hyperaeration

Blood sugar and electrolytes (serum sodium and potassium levels) were also determined as the base line recording. Two solutions, of which one containing salbutamol and another containing normal saline were prepared. There was no detectable difference in colour, smell, or other physical properties between these two solutions. After diagnosing a patient of TTN, candidates were allotted with a study number and his/her TTN score. Respiratory rate, heart rate and oxygen saturation were recorded. These study numbers corresponded to the order of the patient entering the study. Simple random sampling was done according to a computer generated random number table on a master list to one of the two solutions i.e. salbutamol solution and normal saline solution. Then neonate was nebulised with either of the solution. Both the caregiver and the subject were blinded regarding the drug used for nebulization. sample was collected again at 4 hours after nebulization for serum potassium and glucose levels.

Patients received one nebulized dose of either 3ml 0.9% normal saline solution (placebo) or the solution of salbutamol 3 ml (asthalin solution is 5mg/ml) in a normal saline 0.9% solution. The standard dose of salbutamol was calculated according to the weight of the baby i.e. 0.15mg/kg. Solution was given with jet type nebulizer along with continuous flow of oxygen at 5 to 6 litres/min. Administration of the solution was performed by nurse on duty. The dose was administered over 15 minutes, and vital signs were monitored at 30minutes, 1 hour and 4 hours

after nebulization. Intravenous fluids were given as 60ml/kg in enrolled babies and additional oxygen inhalation was given at 2 litres/min through nasal prongs after the nebulization in both cases and control group.

30minutes, 1 hour and 4 hours after nebulization , following parameters were noted like :

- Respiratory rate
- Heart rate
- Oxygen saturation
- TTN score

4 hours after nebulization – blood sample collected for-

- Serum potassium
- Blood Glucose levels

Results

In the present study 65% of the patients were males and 35% were females(figure 1). The mean age of presentation in hours was 3.80 ± 1.77 hours. We also analysed the patient characteristics like gender distribution, age at which the neonate presented to hospital and gestational age (in weeks) at birth. There were no significant differences between the treatment and control groups with regard to any of the following: gestational age (38.35 ± 1.22 vs 38.52 ± 1.26), birth weight, age at admission to hospital (3.80 ± 1.77 in cases and 3.50 ± 1.77 in control group), initial respiratory rate (73.4 ± 4.5 vs 72.2 ± 4.8) and oxygen saturation on admission (94.7 ± 1.6 vs 94.82 ± 1.76). Figure and table 2 shows the result of nebulization in salbutamol and normal saline group in TTN score. There was no significant difference in between two group statistically. Figure and table 3 shows the respiratory rate between two groups after nebulization, statistically it is not significant difference.

Table 1 -TTN SCORE-¹⁰

SCORE	0 POINT	1 POINT	2 POINT	3 POINT
Expiratory grunt	None	Intermittent	Continuous	-
Subcostal retractions	None	Mild	Moderate	Severe
Cyanosis	None	At extremities	Central	-
Nasal flaring	None	Mild	Moderate	Severe
Supraclavicular retractions	None	Mild	Moderate	Severe

Figure 1 shows the distribution of neonates according to gender

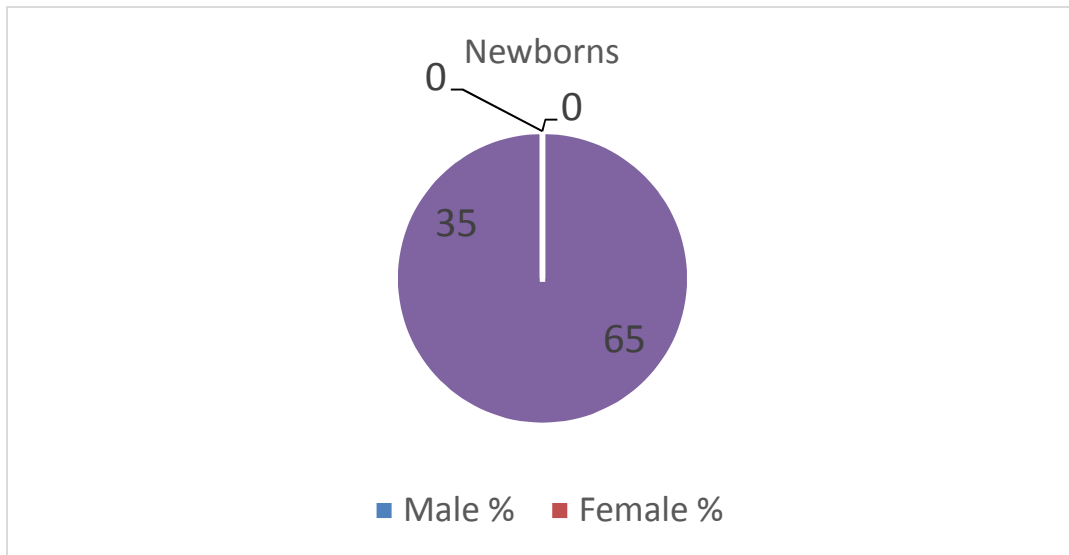


Figure 2: shows the TTN score after nebulization

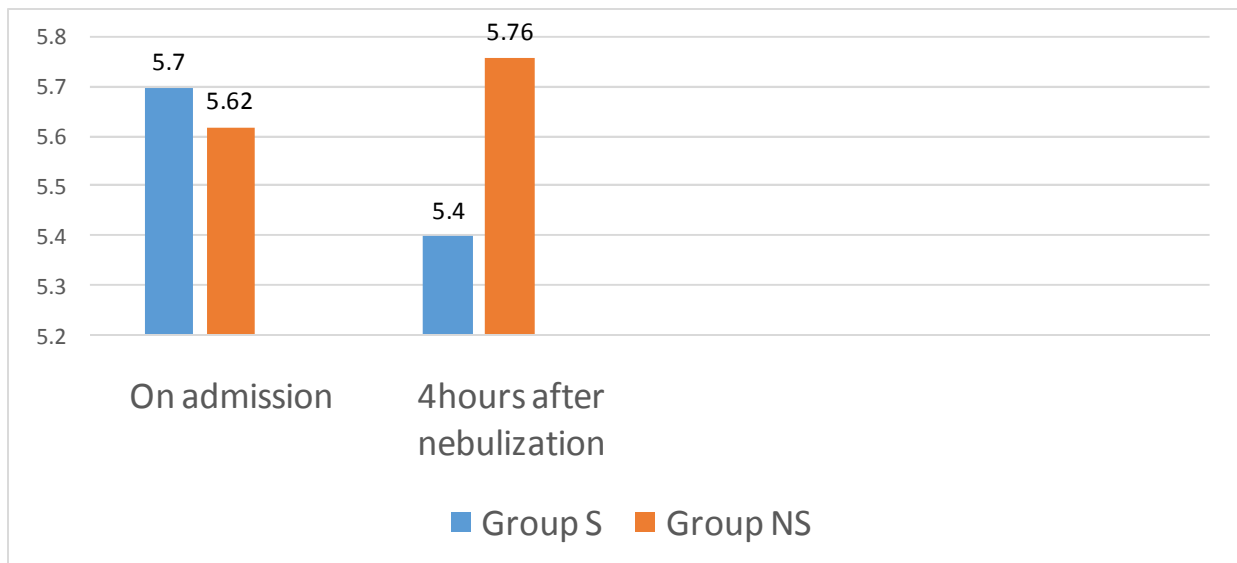


Table 2: Different values of TTN score in groups at different time interval

TTN SCORE	Group S		Group NS		p-value
	Mean	SD	Mean	SD	
On admission	5.700	1.0351	5.620	1.1229	0.712
30 min after nebulization	5.720	1.0506	5.740	1.1214	0.927
1 hour after nebulization	5.500	1.3286	5.700	1.1112	0.416
4 hours after nebulization	5.400	1.4142	5.760	1.1528	0.166

Figure 3 shows the respiratory rate in different groups

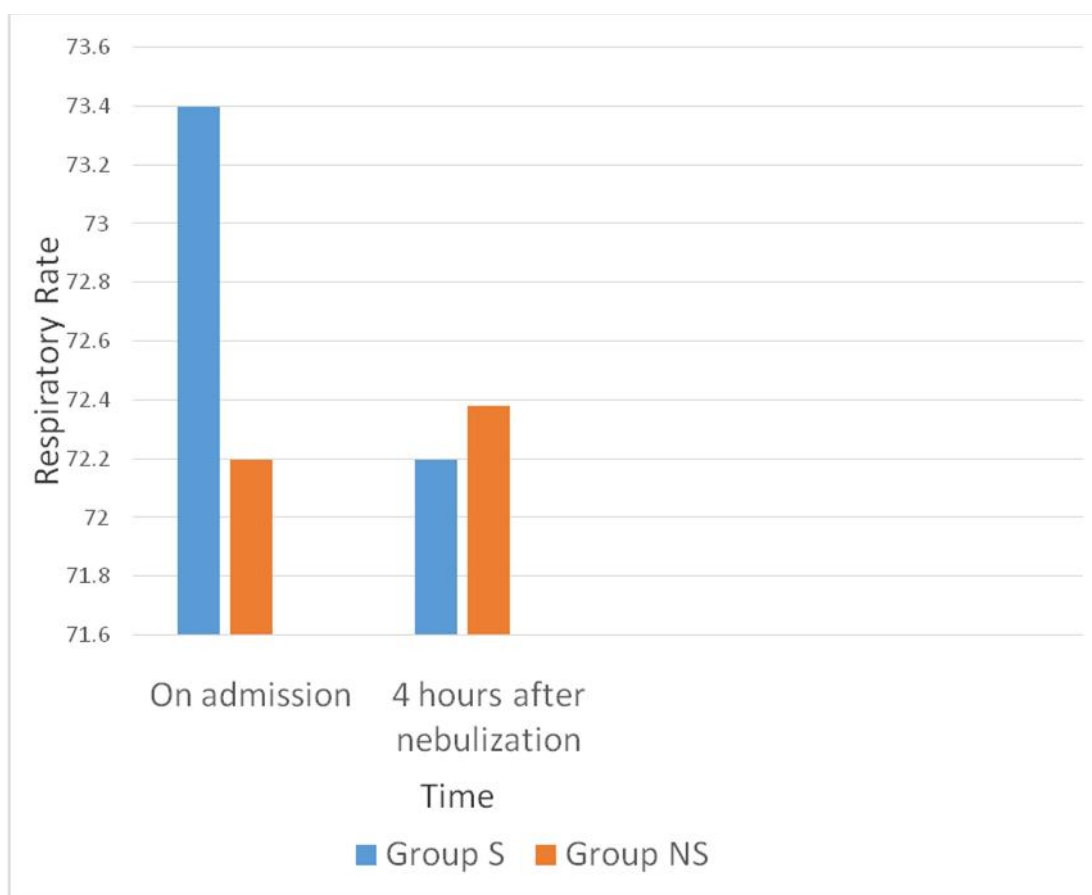


Table 3: Different values of mean (with standard deviation) of respiratory rate in groups at different time interval

Respiratory rate	Group S		Group NS		p-value
	Mean	±SD	Mean	±SD	
On admission	73.400	4.5266	72.200	4.8865	0.206
30 min after nebulization	73.500	4.2342	72.420	5.2648	0.261
1 hour after nebulization	72.900	4.3577	72.280	5.8311	0.548
4 hours after nebulization	72.200	5.1429	72.380	5.5065	0.866

Discussion

Present study was undertaken to see the effect of salbutamol nebulization in transient tachypnea of newborn in the following parameters.

Clinical characteristics

Respiratory rate:

In our study the mean respiratory rate of Salbutamol Group (cases) before nebulization was 73.400 ± 4.5 and it did not decrease significantly 4 hours after nebulization (72.2 ± 5.1). P value was 0.866, which was statistically not significant when we compared it with the respiratory rate of neonates in the control group. This is in contrast to results observed by Armangil D et al¹⁰ which showed significant decrease in respiratory rate (70 ± 19 vs 62 ± 14) and by Venkatamurthy et al¹¹ respiratory rate was (75.74 ± 5.93 and 66.31 ± 7.41) before and after nebulization respectively. Myo Jing Kim et al¹² showed that there was decrease in the duration of tachypnea after treatment with salbutamol nebulization than in the control group (31.3 ± 23.7 h vs. 53.5 ± 56.8 h, respectively); but this difference was not significant ($P=0.37$). However, no differences in the maximum respiratory rates during the acute period after inhalation treatment were observed between the salbutamol inhalation group and the control group.

TTN score:

In our study the mean TTN score before and after 4 hours nebulization in salbutamol group was (5.7 ± 1.0 and 5.40 ± 1.41) and in control group (5.66 ± 1.12 and 5.76 ± 1.15) and it did not decrease significantly with p-value of 0.16. The mean TTN score observed before and after salbutamol nebulization in other studies like Armangil D et al is (8 vs. 2.5) and Venkatamurthy et al (8.26 ± 0.44 vs. 5.77 ± 2.07) showed a decrease in TTN score after nebulization.

Oxygen Saturation:

There was no significant difference with the resultant p-value of 0.32 in the oxygen saturation between the salbutamol (94.78 ± 1.64 on admission and 96.24 after nebulization) and normal saline group (94.82 ± 1.76 on admission and 95.9 ± 1.88).

Average duration of the hospital stay (in days):

Our analysis showed that patients treated with either solution had no significant difference in terms of the duration of hospitalization with p value of >0.05 , these results were in accordance with the study done by Myo Jing Kim et al which also showed that the duration of hospitalization was similar between the 2 groups (8.5 ± 3.9 days vs. 8.8 ± 3.2 days in treatment and control group respectively).

Short term/immediate adverse effects:

Our analysis showed no incidence tachycardia ($>180/\text{min}$) after salbutamol nebulization when compared with normal saline group with p value 0.008. Heart rate evaluated after salbutamol nebulization (137 ± 7.8) showed no significant increase when compared with normal baseline evaluation at the time of admission (135 ± 9.3). Similar results in heart in both treatment and control group after nebulization were shown by the studies done by the Armangil D et al and Venkatamurthy et al.

Specific adverse effect:

Our study showed no significant change in the serum potassium levels and blood glucose levels after salbutamol nebulization when they were compared with the normal saline group.

Studies done by Armangil et al also showed that after nebulization there was no significant change in serum potassium levels in salbutamol and normal saline group respectively.

Conclusion

Thus it can be concluded from the present study that 65% of the patients were males and 35% were females. Group which was nebulized with salbutamol did not show statistically significant improvement in the respiratory rate, TTN score and oxygen saturation when compared with the control group (>0.05). There were no immediate as well as specific side effects observed in the

salbutamol group. Average duration of hospital stay (in days) was almost similar between two groups. Thus, we conclude that our results did not show any significant effect of salbutamol nebulization (single dose) in early resolution of symptoms and early discharge of the baby. There is a need to explore the subject further taking larger sample size with change of dosing schedule to show the efficacy of salbutamol, if any, in treatment of the TTN.

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Conflict of interest: None declared

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