International Journal of Medical Arts 2020; 2 [2]: 457-461.

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main subject [Medicine [Pediatrics]] *

Original article

Inhaled Salbutamol for the Treatment of Transient Tachypnea of the Newborn

Ahmed Abdelaty Salama; Lotfy Abdel-Fattah El-Seheimy; Mohamed Ibrahim Elsamanoudy

Department of Pediatrics, Damietta Faculty of Medicine, Al-Azhar University, Egypt

Corresponding author: **Ahmed Abdelaty Salama**
Email: drahmedsalama@yahoo.com

Submitted at: December 29, 2019; Revised at: April 14, 2020; Accepted at: April 15, 2020; Available online at: April 15, 2020

DOI: 10.21608/ijma.2020.21436.1064

ABSTRACT

Background: Transient tachypnea of the newborn [TTN] is a common physiologic lung disorder. Stimulation of β-adrenergic receptors could alleviate the condition.

Aim of the work: The study was undertaken to assess the efficacy and safety of inhaled salbutamol in reduction of TTN, oxygen treatment and hospitalization.

Patients and Methods: This clinical study included 150 [50 control group, 50 single dose of salbutamol and 50 double-doses of salbutamol] infants between 35th-39th week's gestation. Inhaled salbutamol was given and comparison between the three groups was carried out.

Results: Treatable and control groups were comparable as regard neonatal and maternal characteristics. Heart rate was significantly increased in group B when compared to control group half and one hour after treatment. In addition, respiratory rate was significantly increase in group B when compared to group A at half hour after treatment and continued till 8 hours after treatment. The TTN score after treatment was significantly lower in group B when compared to group A at one hour after nebulized salbutamol and continued till 8 hours. Furthermore, time before initiation of feeding was significantly reduced in group B when compared to group A [26.72[±3.68] vs [39.66[±4.7] and also there was significant reduction of hospitalization days in group B when compared to group A [3.78 [±1.25] vs [7.36[±1.28].

Conclusion: Inhalational salbutamol reduced duration of supplemental oxygen therapy, the duration of hospitalization and time before initiation of feeding, and no adverse effects were reported. Thus, inhaled salbutamol seems to be effective and safe in TTN.

Keywords: Neonate; Salbutamol; Transient; Tachypnea; Nebulized

Please cite this article as: Salama AA, El-Seheimy LA, Elsamanoudy MI. Inhaled Salbutamol for the Treatment of Transient Tachypnea of the Newborn. IJMA 2020; 2[2]: 457-461.

* Main subject and any subcategories have been classified according to researchers' main field of study.

INTRODUCTION

Transient tachypnea of the newborn [TTN] or wet lung is a common physiologic lung disorder characterized by pulmonary edema secondary to clearance delay of fetal alveolar fluid immediately after birth[1]. The exact incidence of TTN is unclear. It is estimated that 0.5% of newborns suffer from wet lung when they are born. According to some epidemiological studies, the incidence of TTN of full-term newborns and premature infant's is 4–5.7% and 10%, respectively. The main high-risk factors include cesarean section, large birth weight, maternal diabetes, maternal asthma, twins, male babies, apneic hypoxia, aspiration of amniotic fluid, over transfusion after birth, delayed umbilical cord ligation[2]

TTN management consists of supportive care, with symptoms generally resolving by 24 to 72 hours of age without significant morbidity. In addition, severe respiratory morbidity and mortality have been reported in some infants [i.e. hypoxia, respiratory distress, and pulmonary air leak], unnecessary antibiotic use, and parental anxiety. The main high-risk factors include cesarean section, large birth weight, maternal diabetes, maternal asthma, twins, male babies, apneic hypoxia, aspiration of amniotic fluid, over transfusion after birth, delayed umbilical cord ligation, patent ductus arteriosus [left-to right shunt and increased pulmonary blood flow increases hydrostatic pressure within blood capillaries of pulmonary vessels, which affects lung fluid clearance], hypoproteinemia , premature birth[3]

Salbutamol is a short-acting, selective Beta2-adrenergic receptor agonist. increase epithelial sodium channel [ENaC] activity to promote lung fluid clearance and this regulates alveolar epithelial Na+ transport by increasing the activity of epithelial Na+-channels [ENaC] and Na+-K+ [4] The significant role of β2AA in promoting resolution of alveolar pulmonary edema was suggested from animal studies and ex vivo human lung studies[5]. However, its use in treatment of management of TTN is not well covered in our institution.

AIM OF THE WORK

This study was to assess the efficacy and safety of inhaled salbutamol in reducing tachypnea, oxygen treatment, and hospitalization for infants with transient tachypnea of the newborn.

PATIENT AND METHODS

This study was conducted at Neonatal Intensive Care unit of Al-Azhar University Hospital [New Damietta] through the period from July 2018 till April 2019.The inclusion criteria were gestational age 35th-39th weeks gestation delivered by cesarean section or vaginal delivery and physical examination and radiologic findings suggesting TTN diagnosis. On the other hand, the newborns with the history of meconium aspiration, respiratory distress syndrome, congenital neonatal pneumonia, polycythemia, hypoglycemia, early sepsis, cardiac disorders, tachycardia [HR>180 b/min], cardiac arrhythmia, and congenital anomaly were excluded from the study.

In our study 150 neonates who were gestational age between 35th -39th week's gestation with TTN were randomly division into three groups the group [A] [control group] received nebulized dose of normal saline solution0.9%, oxygen and IV fluids. However, group [B] received single nebulized dose of salbutamol 0.15 mg/kg in 0.9% saline in addition to oxygen and IV fluids. group [C] received double dose of salbutamo0.15 mg/kg in 0.9% saline solution in addition to oxygen and IV fluids. TTN score before the treatment, 30 and 60 min, and 4 h after nebulization [Table 1].

Table [1]: TTN clinical score. [5]

Score	0 point	1 point	2 points	3 points
Expiratory grunting	None	Intermittent	Continuous	-----
Supraclavicular retraction	None	Mild	Moderate	Severe
Subcostal retraction	None	Mild	Moderate	Severe
Cyanosis	None	At extremities	Central	----
Nasal flaring	None	Mild	Moderate	Severe

Arterial blood gas measured 4 hours after the intervention. The duration of tachypnea, oxygen required, mechanical ventilation, continuous positive airway pressure support, hospital stay, and the time of starting enteral nutrition were observed to assess efficacy of treatment. In this study, all neonates were observed for tachycardia and arrhythmia. Tachy-cardia was known as heart beat more than 180 beats per minute.

Statistical analysis: Data were coded and entered using the statistical package SPSS version 20. Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies [number of cases] and relative frequencies [percentages] for categorical variables. Comparisons between groups were done using unpaired t test when comparing 2 groups. Comparison between values measured

before and after salbutamol in the same group was done using paired t test.

RESULTS

There was no a significant difference between the treatable and control groups in gender, gestational age, weight at birth, maternal history of asthma, delivery type, and 1st -and 5th -minute Apgar score. The lack of significant differences regarding demographic variables between the three groups [Table 2].

With regard to the quantitative nature of the data and their normal distribution, the repeated measure ANOVA was used to compare the means of respiratory and heart rates, Fio2, O2 saturation, and distress scores between the treatment and control groups at different time periods.

There was no statically significant difference in group A regarding HR before 126.8[±6.27]and 4 hours after nebulized 128.8 [±4.5]with P=0.193, there was no statically significant difference in group B regarding HR before 132.4 [±7.78]and 4 hours after nebulized 131.3 [±4.52]]with P=0.567. And also, there was no statically significant difference in group C regarding heart rate before 126.4 [±7] and 4 hours after nebulized 129.28 [±4.7] with P=0.09 [Table 3].

The mean values of the respiratory rate, and TTN score in before and after the initiation of the study was significantly decreased in salbutamol groups [P value < 0.001]. [Tables 4 and 5].

In the salbutamol group the mean values of primary outcomes including duration of oxygen therapy [p value <0.001], duration of admission in hospital [P value= 0.004] and time of starting of enteral feeding [P < 0.001] were significantly lower than in control group. There was statically significant difference between group A and group B as regard to Total Duration on oxygen in hours with p value <0.001, Duration on nasal cannula in hours with p value <0.001 and Duration on Head Box in hour with p value <0.001. There was no significant difference between group B and group C as regard to total duration on oxygen in hour [Table 6]

No kinds of side effects of salbutamol were observed among the neonates since they were checked daily in terms of the Na/K and blood sugar.

Potassium levels were significantly lower in group B when compared to group A at 4 and 8 hours, while the difference between groups B and C was statistically non-significant either at 4 or 8 hours [Table 7].

Table [2]: Comparison of demographic variables between two groups.

Variable		Treatment group		Control group	P value
		Group A	Group B	Group C	
Maternal age [year]		29.84± [4.06]	26.84± [4.1]	28.04± [4.17]	0.080
Gestational Age [week]		38.36 ± [0.76]	38.48 ± [0.87]	37.9± [0.89]	0.040
Birth Weight [Kg]		3.34 ± [0.39]	3.33 ± [0.42]	3.34 ± [0.39]	0.994
Skull Circumference [cm]		34.16 ± [0.85]	33.9 ± [0.53]	33.8 ± [0.66]	0.264
Length [cm]		49.28± [1.29]	49.76± [1.27]	49.44 ± [1.55]	0.541
Sex	Male	[26 [52%	[24 [48%	[22 [44%	0.857
	Female	24 [48%]	26 [52%]	28 [56%]	
Mode of Delivery	Vaginal	12 [24%]	8 [16%]	8 [16%]	
	Cesarean section	38 [76%]	42 [84%]	42 [84%]	0.713

Table [3]: Detailed Description of Heart rate Before and After Nebulized Salbutamol

	Group A Compared to group B			Group B Compared to group C		
	Group A	Group B	P value	Group B	Group C	P value
At admission	126.8[±6.27]	132.4[±7.78]	0.824	132.4[±7.78]	126.4[±7]	0.805
Half hour after administration	126.4	131.36	***0.012****	131.36	130.56	0.673
One hour after administration	129.4[±4.09]	136.36[±5.39]	***0.001****	136.36[±5.39]	135.64[±4,82]	0.784
Four hours after administration	128.8[±4.50]	131.36[±4.52]	0.054	131.36[±4.52]	129.28[±4,71]	0.118
6 hours after administration	129[±4.09]	128.41[±4.60]	0.053	128.41[±4.60]	130.12[±4,68]	0.120
8 hours after administration	129.6[±4.08]	130.26[±4.09]	0.056	130.26[±4.09]	130.73[±4,69]	0.119

Table [4]: Detailed Description of respiratory rate Before and After Nebulized Salbutamol

	Group A Compared to group B			**Group B Compared to group C**		
	Group A	**Group B**		**Group B**	**Group C**	P value
Before nebulized	76[±5.97]	73.24[±5.19]	0.088	73.24[±5.19]	75.32[±4,44]	0.135
Half hour after nebulized	74.2	71.44	***0.015****	71.44	70.92	0.670
One hour after nebulized	70[±4.04]	66.72[±4.88]	***0.014****	66.72[±4.88]	66.64[±4.27]	0.927
Four hours after nebulized	76.28[±4.60]	60.68[±3.86]	***<0.001****	60.68[±3.86]	61.44[±3.91]	0.407
6 hours after nebulized	76.40[±4.58]	59.56[±3.84]	***<0.001****	59.56[±3.84]	60.43[±3.87]	0.403
8 hours after nebulized	76.15[±4.40]	59.65[±3.82]	***<0.001****	59.65[±3.82]	59.71[±3.85]	0.401

Table [5]: Detailed Description of TTN score Before and After Nebulized Salbutamol

	Group A Compared to group B			Group B Compared to group C		
	Group A	Group B		Group B	Group C	P value
Before salbutamol	7.72[±0.89]	7.68[±0,98]	0.881	7.68[±0,98]	7.76[±0,59]	0.731
30 min after nebulized	7.48	7.08	0.109	7.08	7.12	1.000
One hour after nebulized	6.48[±0.51]	5.84[±0.94]	***0.005****	5.84[±,94]	5.84[±,85]	1.000
Four hours after nebulized	7.6[±1]	4.28[±1.13]	***<.001****	4.28[±1,13]	4.56[±1,04]	0.369
6 hours after nebulized	7.5[±.87]	4.26[±1.17]	***<.001****	4.26[±1,17]	4.54[±1,03]	0.360
8 hours after nebulized	7.6[±.88]	4,25[±1.16]	***<.001****	4,25[±1,16]	4,55[±1,04]	0.401

Table [6]: Level of Respiratory Support and 2nd outcome For Studied groups.

		Group A Compared to group B			**Group B Compared to group C**		
		Group A [n=50]	Group B [n=50]	P value	Group B [n=50]	Group C [n=50]	P value
		Count [%]	Count [%]		Count [%]	Count [%]	
Level of Respiratory Support [after 30 min]	CPAP	24 [48%]	28 [56%]	0.772	28 [56%]	22 [44%]	0.572
	Nasal	26 [52%]	22 [44%]		22 [44%]	28[56%]	
Level of Respiratory Support [after1hour]	CPAP	20 [40%]	14 [28%]	0.769	14 [28%]	18 [32%]	1.00
	Nasal	30 [60%]	36[72%]		36[72%]	32 [64%]	
Level of Respiratory Support [after 4 Hours]	CPAP	16 [32%]	12[24%]	0.754	12[24%]	12 [24%]	1.00
	Nasal	34 [68%]	38[76%]		38[76%]	38 [76%]	
Time before initiation of feeding [Hours]		39.66[±4.7]	26.72[±3.68]	***0.001****	26.72[±3.68]	26.56[±3.47]	0.906
Days of hospitalization		7.36[±1.28]	3.78 [±1.25]	***0.005****	3.78 [±1.25]	3.35 [±1.05]	0.808

Table [7]: Data of Electrolytes after administration

	Group A Compared to group B			Group B Compared to group C		
	Group A	Group B	P value	Group B	Group C	P value
K 4h	4.47 ± [0.42]	3.75 ± [0.3]	< 0.001*	3.75 ± [0.3]	3.77 ± [0.26]	0.447
K 8h	4.46 ± [0.41]	3.92 ± [0.5]	< 0.001*	3.92 ± [0.5]	3.71 ± [0.29]	0.443

DISUCSSION

The TTN is due to delay in intra pulmonary fluid resorption and it is an important diagnosis with a dilemma of therapy in NICU, the most common clinical presentation of TTN is tachypnea, which presents during the first and second hours after birth. Breathing can reach up to 60-120 breath/minute[6].

The inability of the fetal lung that switch trans epithelial liquid flow from secretion to absorption at birth. and the fact that increase in ENaC expression are seen only in late gestation. may play an important role in the development of TTN[7].

Persistent tachypnea can lead to the increase in hospital stay duration, antibiotic therapy, and parent anxiety[8].

Although the common use of beta-2A in treatment of neonatal chest problem in premature infants, few studies recommended the dosage, duration, efficacy and safety of used inhaled beta-2A in the management of neonatal respiratory disease[9].

The primary objective in our study was to assess the efficacy and safety of inhaled salbutamol in reducing tachypnea, oxygen treatment, time of initiation of enteral feeding and hospitalization for infants with transient tachypnea of the newborn.

This study showed that the duration of tachypnea, hospitalization, oxygen required, and the time of starting enteral feeding were shorter in the salbutamol group than the control group and there is no Significant difference between single and double dose. Moreover, the Fio_2 and Pco_2 decreased; however, O_2 saturation and Pao_2 increased over time in the salbutamol group.

Armangil et al.[5] showed that salbutamol can decrease hospital stay duration among neonates diagnosed with TTN and the results are consistent with the findings of this study [P<0.05]. The same results have been found by Armangil et al. in relation to salbutamol effects on respiratory rates; however, in this study, no statistically significant differences were observed in this regard [P>0.05].

Mohammadzadeh et al.[10] showed that inhaled salbutamol can significantly decrease the time of oxygen therapy, initiation of feeding and hospitalization. The obtained results are similar with the findings in our study [P<0.05]. As the previous studies showed no neonates experienced any kinds of salbutamol side effects[5,10].

Kim et al.[11] reported that inhaled salbutamol can result in decrease duration of tachypnea and subsequently shorter duration of oxygen and antibiotic therapy. However, no significant reduction in the hospitalization was observed.

In the present study, a significant decrease was observed in the hospitalization in the salbutamol group [P<0.001]. Mousavi et al.[12] showed that administration of salbutamol can result in the significant reduction of respiratory distress score which was consistent with the results obtained from this study [P<0.05].

In the aforementioned study, the final amount of Pco_2 in the case group increased; however, it was not significant. In the present study, this amount had significantly decreased in the case group [P< 0.05]

Conclusion: The administration of Inhaled salbutamol was effective with respect to both clinical and laboratory findings of TTN and without any adverse side effect. The administration of salbutamol can significantly improve TTN. It reduces the time of hospitalization, the day of initiation the enteric feeding, and the duration of tachypnea. Further studies examining a larger number of patients with strict control over dosage and frequency of salbutamol inhalations are necessary to better direct the treatment of TTN.

Financial and Non-Financial Relationships and Activities of Interest

None

REFERENCES

1. **Eghbalian F, Sabzehei MK, Emamzadeh N, Shokouhi M, Basiri B, Faradmal J, Salavati J.** Comparison of Restricted Fluid Volume with Standard Fluid Volume in Management of Transient Tachypnea of the Newborns: A Randomized Controlled Trial. Int J Pediatr. **2018**;6[9]: 8289-96. [DOI: 10.22038/IJP.2018. 30462.2677].
2. **Pramanik AK, Rangaswamy N, Gates T.** Neonatal respiratory distress: a practical approach to its diagnosis and management. Pediatr Clin. **2015**;62[2]:453-69. [DOI: 10.1016/j.pcl.2014.11.008].
3. **Andrzejowski P, Carroll W.** Salbutamol in paediatrics: pharmacology, prescribing and controversies. Arch Dis Child Educ Pract Ed. **2016**;101[4]:194-7. [DOI: 10.1136/ archdischild-2014-307285].
4. **Armangil D, Yurdakök M, Korkmaz A, Yiğit Ş, Tekinalp G.** Inhaled beta-2 agonist salbutamol for the treatment of transient tachypnea of the newborn. J Pediatr. **2011**; 159 [3]: 398-403. [DOI: 10.1016/j.jpeds.2011.02.028].
5. **Moresco L, Bruschettini M, Cohen A, Gaiero A, Calevo MG.** Salbutamol for transient tachypnea of the newborn. Cochrane Database Syst Rev. **2016**;(5):CD011878. [DOI: 10.1002/14651858].
6. **Davies JC.** Ion transport in lung disease. Pediatric pulmonology. Supplement. **2004**; 26: 147. [DOI: 10.1002 / ppul.70087].
7. **Harding R, Hooper SB.** Regulation of lung expansion and lung growth before birth. J Applied Physiol. **1996**; 81 [1]: 209-24. [DOI:10.1152/jappl.1996.81.1.209].
8. **Patel H, Gouin S, Platt RW.** Randomized, double-blind, placebo-controlled trial of oral albuterol in infants with mild-to-moderate acute viral bronchiolitis. J Pediatr. **2003**; 142 [5]: 509-14. [DOI: 10.1067/mpd.2003.196].
9. **Mohammadzadeh I, Akbarian-Rad Z, Heidari F, Zahedpasha Y, Haghshenas-Mojaveri M.** The effect of inhaled salbutamol in transient of tachypnea of the newborn: a randomized clinical trial. Iranian J Pediatri. **2017**; 27[5]. [DOI:10.5812/ijp.9633].
10. **Kim MJ, Yoo JH, Jung JA, Byun SY.** The effects of inhaled albuterol in transient tachypnea of the newborn. Allergy Asthma Immunol Res. **2014** Mar;6(2):126-30. [DOI: 10.4168/aair.2014.6.2.126].
11. **Mussavi M, Asadollahi K, Kayvan M, Sadeghvand S.** Effects of nebulized albuterol in transient tachypnea of the newborn a clinical trial. Iranian J Pediatr. **2017**; 27(3): e8211. [DOI: 10.5812/ijp.8211].