Effects of Inhaled Salbutamol on Transient Tachypnea of the Newborn

Behnaz Basiri, Nishteman Sadeghi, Mohammad Kazem Sabzehei, and Farzaneh Esna Ashari

BACKGROUND: One of the most common causes of respiratory distress in newborns is transient tachypnea of the newborn (TTN). Salbutamol is often suggested to increase the rate of pulmonary fluid absorption in newborns with TTN. This study aimed to evaluate the efficacy of inhaled salbutamol in TTN management. METHODS: This double-blind clinical trial was conducted on 52 newborns admitted to the neonatal ICU of Fatemieh Hospital of Hamadan, Iran. The newborns were randomly assigned to 2 groups of equal members: one group received 2 mL of nebulized sodium chloride concentration (control group), and the other group was treated with 0.1 mg/kg of salbutamol (treatment group). The clinical outcomes were then compared before and 0.5, 1, and 4 h after the intervention. The data were recorded in a checklist and then were statistically analyzed in SPSS 16: the significant level was decided to be $P < .05$. RESULTS: The comparison of TTN scores revealed a significant difference between the 2 groups 1 h ($P = .005$) and 4 h ($P < .001$ per Table 3) after the intervention. Moreover, the mean F_{IO_2} 1 h after the intervention was 53.3 ± 6.6 in the treatment group and 57.7 ± 7.5 in the control group ($P = .02$). The mean duration of respiratory support in the treatment and control groups was 2.4 ± 2.7 and 3.1 ± 0.8 d, respectively, ($P = .002$). The findings suggested no statistically significant difference between the 2 groups regarding the adverse effects, length of stay (LOS), duration of antibiotics intake, oral feeding resumption time, and maximum oral feeding time ($P > .05$ for all). CONCLUSIONS: The study results indicated that inhaled salbutamol significantly decreased the TTN clinical score, oxygen demands, and duration of respiratory support, whereas there was no significant difference between the groups in terms of LOS. *Key words: newborns; respiratory distress; salbutamol; transient tachypnea.* [Respir Care 2022;67(4):433–439. © 2022 Daedalus Enterprises]

Introduction

Transient tachypnea of the newborn (TTN) is one of the most common respiratory problems caused by inadequate or delayed clearance of fetal pulmonary fluid.[1] It is characterized by a breathing frequency > 60 breaths/min and respiratory distress manifested by grunting, flaring, and retractions.[2] This condition necessitates the admission of newborns to the neonatal ICU (NICU), the administration of antibiotics, mechanical ventilation, and mother-child separation which can lead to breastfeeding difficulties.[3]

The incidence of TTN ranges 0.5–2.8% in all deliveries.[4] Male gender, macrosomia, gestational diabetes, gestational asthma, preterm birth, perinatal asphyxia, and Cesarean sections are the main risk factors for TTN.[5] Previous studies have reported that the risk of TTN in preterm newborns was higher than in term infants. This was especially more common in newborns delivered through Cesarean sections.[6] In general, newborns with TTN need to be admitted to NICUs.[7] A chest x-ray can be used to diagnose TTN. This method demonstrates an increase in diffuse parenchymal infiltrates caused by fluid in the interstitium, interlobar fissures, and, occasionally, pleural effusions.[8] The most common methods for diagnosing and monitoring TTN are chest radiography, laboratory tests, and close cardiorespiratory monitoring.[9]

The clinical features of TTN manifest shortly after birth or a few hours later. This situation arises because of the newborn's inability to absorb pulmonary fluid and immaturity in the expression of the epithelial Na^+ channels (ENaC). The fetal catecholamines activated through β-adrenergic receptors, active sodium (Na^+) absorption via enhanced ENaC, and sodium-potassium adenosine triphosphatase activity all influence pulmonary fluid release. By

increasing the activity of ENaC and Na^+/K^+-ATPase, β-2 adrenergic agonists can stimulate the β-adrenergic receptors for the regulation of active Na^+ transport required to remove excess fluid from alveolar air space.[10] It is noteworthy that β2AA plays a vital role in increasing the resolution of alveolar pulmonary edema. As a β2AA, inhaled salbutamol is recommended to be used to increase the rate of fetal pulmonary fluid absorption in newborns with TTN. This study aimed to evaluate the efficacy of inhaled salbutamol in TTN management and to investigate whether inhaled salbutamol is a safe medicine for newborns with TTN.

QUICK LOOK

Current knowledge

Transient tachypnea of the newborn (TTN) is one of the most common respiratory problems caused by inadequate or delayed clearance of fetal pulmonary fluid. Although salbutamol may reduce length of stay, it is not known that whether it can reduce the need for oxygen therapy and the duration of tachypnea.

What this paper contributes to our knowledge

The results showed an increase in oxygen saturation and a decrease in the transient tachypnea of the newborn (TTN) clinical score and duration of respiratory support after the administration of salbutamol. These findings suggested that β-2 adrenergic agonists could be an effective treatment option for TTN.

Methods

A double-blind clinical trial was conducted on 52 newborns admitted to the NICU of Fatemieh Hospital of Hamadan, Iran.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) gestational age 34–37 weeks; (2) tachypnea with $>$ 60 breaths/min during the first 6 h of life, continuing for 12 h; and (3) diagnosis of TTN based on chest x-ray findings, including at least one of the following signs: lung hyperinflation, prominent vascular/perihilar marking, fluid-filled interlobar fissure, fluffy bilateral infiltration, and pulmonary edema.

The exclusion criteria were also as follows: (1) respiratory distress syndrome (reticulogranular patterns or white lung on chest x-ray or surfactant use), (2) meconium aspiration syndrome (history of meconium disposal or patchy infiltration on chest x-ray), (3) sepsis (prenatal infection risk factors, 5,000 $<$ white blood cells $>$ 15,000/mm^3, positive C-reactive protein, positive blood culture, and focal infiltration on chest x-ray), (4) congenital heart defects (based on echocardiography), (5) nonrespiratory causes of tachypnea (ie, hypocalcemia, persistent hypoglycemia, and polycythemia), (6) the history of maternal substance abuse, and (7) death during the study.

Study Design

Assuming the size effect of 0.80 for length of stay (LOS) in NICU, an alpha error of 0.05, and a test power of 80%, the sample size was determined to be 26 in each group. The required data, including chest radiograph, echocardiography, serum biochemistry (ie, glucose and calcium), and hemoglobin level, were collected from all participants. The purposive sampling method was used to select the participants. The randomization process was carried out using the permuted block randomization method. The block size and allocation ratio for this purpose were 5 and 1:1, respectively. Before assigning the participants to 2 groups, the random allocation sequence was concealed in sealed opaque envelopes. The evaluator was blinded to the evaluation processes in this study, and the newborns were randomly divided into 2 groups. It is worth noting that the specialists in this study were not aware of the medications (sodium chloride alone or a combination of sodium chloride and salbutamol).

The data were collected using the special demographics and clinical information forms and recorded in a researcher-made checklist. A total of 60 newborns with TTN entered the study, but 8 (4 from the control group and 4 from the treatment group) were excluded from the study during the intervention for several reasons, including cardiovascular diseases, sepsis, and respiratory stress disorder. It is noteworthy that no cases were excluded due to tachycardia or death. Finally, a total of 52 newborns (n = 26 in each group) continued the study to the end (Fig. 1). Based on Rawlings and Smith criteria, tachypnea was identified as the principal manifestation of TTN.[2]

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The authors have disclosed no conflicts of interest.

There was no funding for the study.

This study was registered at the Iranian Registry for Clinical Trials (Code: IRCT201711139014N201).

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DOI: 10.4187/respcare.09284

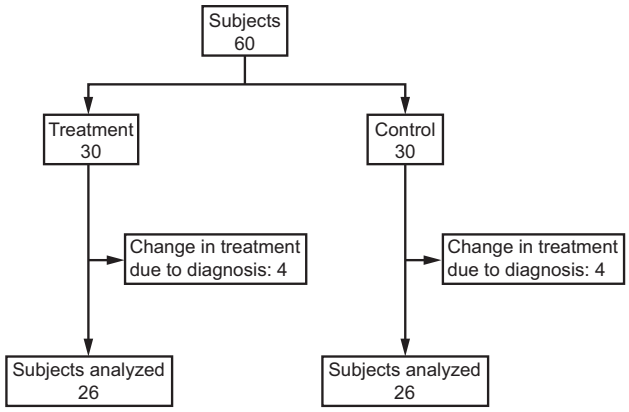

Fig. 1. Flow chart.

Table 1. Clinical Scoring of Transient Tachypnea of the Newborn

Score	0 Points	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

2 mL of 0.9% sodium chloride (Ghazi Pharmaceutical Company, Tehran, Iran) was administered to participants in the control group. Those in the treatment group received 0.1 mg/kg body weight of salbutamol (Cipla, Mumbai, India) combined with 2 mL of 0.9% sodium chloride. Both administrations were performed using a nebulizer under an oxygen flow of 5–6 L/min for 20 min.

Nebulization was given 12 h after birth for the first time. The vital signs, clinical TTN score (based on expiratory grunting, supraclavicular retractions, subcostal retractions, cyanosis, and nasal flaring) (ranging between 0–3 as shown in Table 1), and breathing frequency were assessed 0.5, 1, and 4 h after the intervention.[3] All data were recorded in a checklist.

Respiratory support was initiated at the predetermined time using respiratory protection approaches, including no oxygen, intra-incubator oxygen (30%), hood (40%), a nasal cannula (50% or 5 L/min), and nasal CPAP (50–60% with 5 cm H_2O). These items were determined based on the neonatal conditions. All the participants were visited and monitored daily before and after the intervention for measuring and recording the intended variables.

Statistical Analysis

SPSS Statistics (version 16, IBM, Armonk, New York) was used to analyze the collected data and perform statistical tests. The Student *t* test or Mann-Whitney U test was employed to compare the newborns before and after the intervention. The repeated measures analysis of variance (ANOVA) was also used to compare the mean TTN score with the pre- and post-intervention breathing frequency, the F_{IO_2}, and oxygen saturation level. The significance level was decided to be $P < .05$.

Ethical Considerations

The study protocol was approved by the ethics committee of Hamadan University of Medical Sciences, Iran, (No. IR.UMSHA.REC.1396.531). In addition, the parents of newborns were fully briefed on the research objectives, procedures, and techniques, and they were assured that their newborns' information would be kept confidential. An informed consent form was also obtained from the parents of newborns.

Results

This study was conducted on 52 newborns with TTN who were randomly assigned to treatment and control groups. There was no statistically significant difference between the 2 groups in terms of gender, gestational age, birthweight, maternal diseases, delivery type, and the first- and fifth-min Apgar score (Table 2).

Table 3 shows the results of comparing the 2 groups regarding TTN score, breathing frequency, oxygen saturation, F_{IO_2}, and S_{pO_2}/F_{IO_2}. The results indicated that there was no statistically significant difference between the 2 groups before the intervention ($P > .05$ for all). Moreover, no statistically significant difference was found between the groups in the above-mentioned variables half an hour after the intervention, except for the oxygen saturation that was significantly higher in the treatment group ($P = .01$). The results also demonstrated that the mean TTN score, breathing frequency, and F_{IO_2} were significantly lower, and oxygen saturation and S_{pO_2}/F_{IO_2} were significantly higher in the treatment group 1 h and 4 h after the intervention ($P < .05$ for all).

Table 4 summarizes other clinical parameters. No adverse effect was observed in either of the groups. The repeated measure ANOVA was employed to compare the treatment and control groups in the mean TTN score, respiratory frequency, O_2 saturation, and F_{IO_2} at different times. The ANOVA test results revealed a significant difference between the 2 groups in the TTN score ($P = .035$, Fig. 2), breathing frequency ($P < .003$, Fig. 3), O_2 saturation ($P < .001$, Fig. 4), and F_{IO_2} ($P = .029$, Fig. 5).

Discussion

TTN is a significant diagnosis with a treatment dilemma in the NICU. Although the precise pathology of the condition is unknown, it is most commonly caused by delayed reabsorption of intrapulmonary fluid.[11] The mechanism of

Table 2. Comparison of Demographic Variables Between 2 Groups

Variables	Treatment Group	Control Group	*P*
Gender			
Male	46.2	57.7	.37
Female	53.8	42.3	
Gestational age, weeks	36.31 ± 1.87	36.58 ± 1.47	.57
Birthweight, g	2,873.69 ± 580.37	2,772 ± 469.74	.66
Apgar score first, min	7.92 ± 0.69	8.11 ± 0.59	.28
Apgar score fifth, min	8.96 ± 0.66	9.11 ± 0.59	.38
Mode of delivery			
Cesarean section	38.50	57.70	.17
Vaginal delivery	61.50	42.30	
Maternal disease			
Yes	30.8	34.6	.76
No	39.2	65.4	
Type of respiratory support			
No oxygen	0	0	.53
Intra-incubator oxygen	3.85	15.38	
Hood	42.31	38.46	
Nasal cannula	26.92	26.92	
Nasal CPAP	26.92	19.23	

Table 3. Comparison of Clinical Parameters Between Groups

Variable	Treatment Group	Control Group	*P*
TTN score			
Before treatment	2.08 ± 0.85	2.00 ± 0.69	.80
0.5 h after the intervention	1.54 ± 0.90	1.34 ± 0.56	.66
1 h after the intervention	0.73 ± 0.78	1.27 ± 0.60	.005
4 h after the intervention	0	0.88 ± 0.59	< .001
Breathing frequency			
Before treatment	76.23 ± 6.08	77.46 ± 6.87	.49
0.5 h after the intervention	72.27 ± 5.27	74.88 ± 6.14	.11
1 h after the intervention	68.81 ± 3.79	74.31 ± 6.14	< .001
4 h after the intervention	64.81 ± 2.84	68.59 ± 5.99	< .001
S_{pO_2} saturation, %			
Before treatment	91.42 ± 1.53	91.24 ± 1.63	.66
0.5 h after the intervention	92.34 ± 1.49	91.23 ± 1.53	.01
1 h after the intervention	93.73 ± 1.80	92.65 ± 1.32	.01
4 h after the intervention	95.34 ± 1.06	92.53 ± 1.30	.008
F_{IO_2}			
Before treatment	64.74 ± 8.59	62.50 ± 8.86	.98
0.5 h after the intervention	58.41 ± 7.58	61.74 ± 8.59	.15
1 h after the intervention	53.27 ± 6.63	57.69 ± 7.51	.03
4 h after the intervention	45.38 ± 7.20	56.34 ± 7.69	< .001
S_{pO_2}/F_{IO_2}			
0.5 h after the intervention	159.01 ± 23.31	151.13 ± 24.75	.24
1 h after the intervention	176.07 ± 23.23	161.07 ± 24.00	.03
4 h after the intervention	206.11 ± 48.83	167.40 ± 23.09	.001

TTN = transient tachypnea of the newborn

Table 4. Comparison of Outcomes Between 2 Groups

Variables, d	Treatment Group	Control Group	*P*
Duration of respiratory support	2.42 ± 0.70	3.15 ± 0.83	.002
Length of hospital stay	6.31 ± 1.05	5.77 ± 1.11	.08
Duration of antibiotic therapy	5.46 ± 1.14	5.23 ± 1.24	.48
Time to start oral feeding	2.35 ± 0.48	2.27 ± 0.45	.55
Maximum oral feeding time	4.31 ± 0.55	4.19 ± 0.57	.46

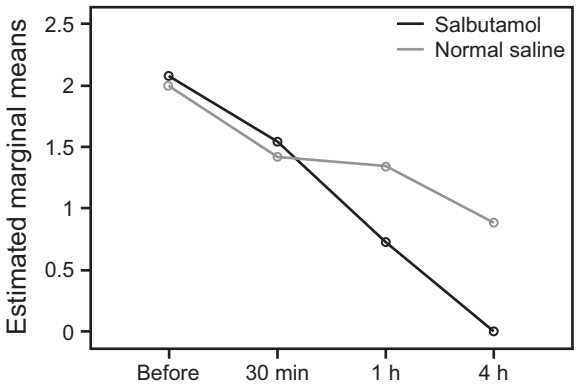

Fig. 2. Mean transient tachypnea of the newborn score in treatment and control groups at each time period.

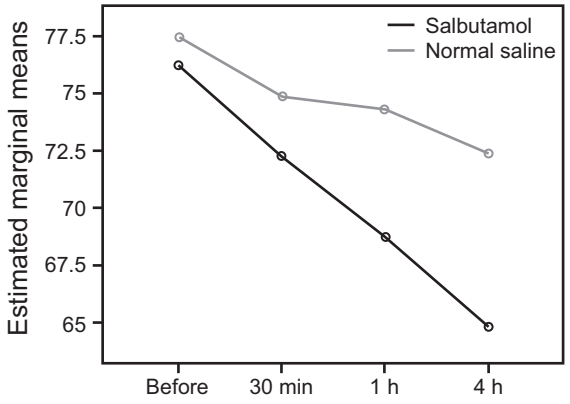

Fig. 3. Mean breathing frequency in treatment and control groups at each time period.

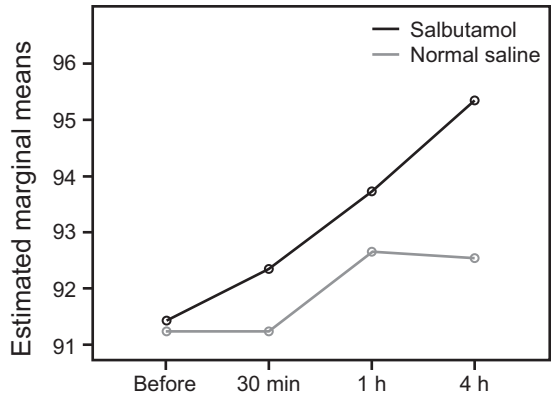

Fig. 4. Mean oxygen saturation in treatment and control groups at each time period.

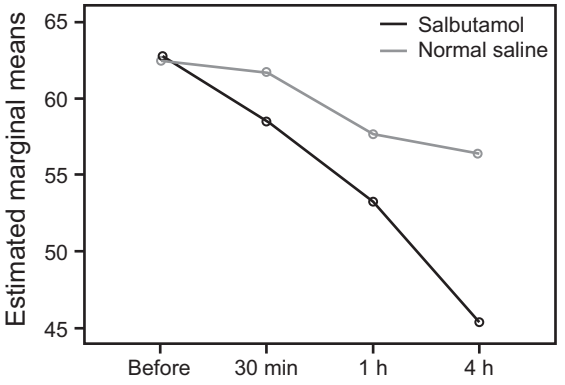

Fig. 5. Mean F_{IO_2} in treatment and control groups at each time period.

pulmonary fluid transepithelial movement is described based on adrenergic stimulation at birth. The amiloride-sensitive ENaC-mediated alveolar fluid is stimulated by cyclic adenosine monophosphate and $Ca2^{+}$.[12,13] The transport of pulmonary fluid into the pulmonary circulation is caused by the movement of Na^{+} through the interstitium.[12] In newborns with TTN, pulmonary fluid resorption is delayed. The presence of excess pulmonary water in this clinical syndrome contributes to a decrease in pulmonary compliance. Tachypnea and increased work of breathing compensate for it. The β-2 agonist's therapeutic role in the treatment of pulmonary edema is to speed up the secretion of excess fluid from the alveolar space. It is accomplished by increasing the function of epithelial transporter proteins. Fluid restriction could be beneficial in the treatment of newborns with severe TTN.[14]

Based on these findings, we hypothesized that salbutamol stimulates lung fluid reabsorption in newborns with TTN, and we investigated the effects of inhaled salbutamol on the clinical outcomes of such newborns.

The study results indicated that inhaled salbutamol reduced the duration of symptoms and respiratory support in newborns with TTN.

Consistent with the findings of this study, several studies have confirmed the effect of inhaled salbutamol on the TTN clinical score.[15-19] Similar to Armangil et al,[3] we employed the Rawlings and Smith criteria to evaluate the TTN score. Nevertheless, the post-intervention TTN score in this study was smaller than the score reported by the above-mentioned study. This discrepancy can be attributed to the differences in the drug dosages. Moreover, salbutamol was administered to

participants based on their body weight in this study, whereas they administered a constant dose for all participants.

The most important complication of TTN is tachypnea, which occurs 1–2 h after delivery and can be severe, reaching 60–120 breaths/min. Prolonged tachypnea can cause a delay in starting enteral feeding, an increase in LOS, and unnecessary antibiotic administration.[9] Kim et al demonstrated that the administration of salbutamol after lung surgery resolved pulmonary edema and improved blood oxygenation in high-risk participants.[11] Ex vivo evidence obtained from human and animal models indicates that exogenous β2AA stimulates pulmonary fluid absorption.[10,20] Salbutamol, as a β2AA, can increase pulmonary fluid absorption. The study findings, as well as evidence from related studies, demonstrated that β2AA was an effective treatment option for TTN management.[3,11,18,19] It can help to lessen the severity of tachypnea over time.

This study showed that the F_{IO_2} decreased and O_2 saturation increased over time in the treatment group, which is consistent with the findings of some previous studies.[16,18,21] The duration and demand for respiratory support were significantly lower in the treatment group than in the control group in this study. This is consistent with the finding of other similar studies.[19,22-24]

The study results indicated no significant difference between the 2 groups in LOS, which is consistent with the findings of a similar study by Kim et al.[11] However, most studies have shown that salbutamol reduces LOS.[18,19] This difference can be attributed to neonatal conditions or other confounding variables, such as the male gender[17,25] and route of delivery.[26] This study was focused on minimizing the effects of these intervening variables by matching the groups. It is critical to have therapeutic options available to reduce LOS. However, more comprehensive studies are needed before prescribing inhaled β2AA as a routine treatment for TTN.[27]

Serious bronchospasm, arrhythmia, hypokalemia, and hyperglycemia caused by glycogenolysis have rarely been reported as adverse effects of salbutamol.[28,29] It should be noted that no adverse effect was observed after the administration of salbutamol, which has been confirmed by some similar studies.[17,19,25] Although some other studies have reported contradictory findings,[19] salbutamol inhalation is believed to be a low-risk treatment for TTN.

Limitations

The small sample size and the lack of other treatment methods were the main limitations of this study. As a result, it is recommended that more comprehensive studies be conducted to confirm the efficacy of inhaled salbutamol as a therapeutic intervention in TTN patients. This study represented a method for gaining new insights into the efficacy of salbutamol in combination with sodium chloride. Instead of using fixed doses, this method proposes administering doses based on the patient's body weight to increase oxygen saturation and lower the TTN clinical score.

Conclusions

The study findings suggested that inhaled salbutamol significantly decreased the TTN clinical score, breathing frequency, F_{IO_2}, and duration of respiratory support, whereas there was no significant difference between the 2 groups in terms of LOS and time of enteral feeding. Therefore, a combination of inhaled salbutamol and routine care is recommended to be prescribed for newborns with TTN to improve respiratory distresses and their clinical consequences.

REFERENCES

1. MacIntyre NR, Galvin WF, Mishoe SC. Respiratory Care: Principles and Practice. Burlington, MA: Jones & Bartlett Learning; 2015: 96-98.
2. Hagen E, Chu A, Lew C. Transient tachypnea of the newborn. NeoReviews 2017;18(3):e141-e148.
3. Armangil D, Yurdakök M, Korkmaz A, Yiğit S, Tekinalp G. Inhaled beta-2 agonist salbutamol for the treatment of transient tachypnea of the newborn. J Pediatr 2011;159(3):398-403.e1.
4. Wells RG. Diagnostic Imaging of Infants and Children: McGraw-Hill Education; 2012.
5. Altman M, Vanpée M, Cnattingius S, Norman M. Risk factors for acute respiratory morbidity in moderately preterm infants. Paediatr Perinat Epidemiol 2013;27(2):172-181.
6. Zanardo V, Simbi AK, Franzoi M, Soldà G, Salvadori A, Trevisanuto D. Neonatal respiratory morbidity risk and mode of delivery at term: influence of timing of elective cesarean delivery. Acta Paediatr 2004;93(5):643-647.
7. Reuter S, Moser C, Baack M. Respiratory distress in the newborn. Pediatr Rev 2014;35(10):417-429.
8. Buchiboyina A, Jasani B, Deshmukh M, Patole S. Strategies for managing transient tachypnoea of the newborn - a systematic review. J Matern Fetal Neonatal Med 2017;30(13):1524-1532.
9. Moresco L, Bruschettini M, Cohen A, Gaiero A, Calevo MG. Salbutamol for transient tachypnea of the newborn. Cochrane Database Syst Rev 2021;2(5):CD011878.
10. Mutlu GM, Factor P. Alveolar epithelial beta2-adrenergic receptors. Am J Respir Cell Mol Biol 2008;38(2):127-134.
11. Kim MJ, Yoo JH, Jung JA, Byun SY. The effects of inhaled albuterol in transient tachypnea of the newborn. Allergy Asthma Immunol Res 2014;6(2):126-130.
12. Bland RD, Carlton DP, Jain L. Lung fluid balance during development and in neonatal lung disease. In: Bancalari E, Polin RA, editors. The newborn lung neonatology questions and controversies. Philadelphia, PA: Saunders Elsevier; 2008: 141-165.
13. Bancalari E. The Newborn Lung: Neonatology Questions and Controversies E-Book: Elsevier Health Sciences; 2012.
14. Stroustrup A, Trasande L, Holzman IR. Randomized controlled trial of restrictive fluid management in transient tachypnea of the newborn. J Pediatr 2012;160(1):38-43.
15. Keleş E, Gebeşçe A, Demirdöven M, Yazgan H, Baştürk B, Tonbul A. The effects of inhaled β-adrenergic agonists in transient tachypnea of the newborn. Glob Pediatr Health 2016;3:2333794X1664525.

16. Mussavi M, Asadollahi K, Kayvan M, Sadeghvand S. Effects of nebulized albuterol in transient tachypnea of the newborn: a clinical trial. Iran J Pediatr 2017;27(3):e8211.
17. Nawar F, Aly H, Helmy S, El Monaem M. Is salbutamol and adrenalin inhalation effective in management of transient tachypnea of newborn? BJMMR 2016;14(3):1-8.
18. 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. Iran J Pediatr 2017;27(5):e9633.
19. Salama AA, El-Seheimy LA, Elsamanoudy MI. Inhaled salbutamol for the treatment of transient tachypnea of the newborn. IJMA 2020;2 (2):457-461.
20. Ronca AE, Abel RA, Ronan PJ, Renner KJ, Alberts JR. Effects of labor contractions on catecholamine release and breathing frequency in newborn rats. Behav Neurosci 2006;120(6):1308-1314.
21. Licker M, Tschopp JM, Robert J, Frey JG, Diaper J, Ellenberger C. Aerosolized salbutamol accelerates the resolution of pulmonary edema after lung resection. Chest 2008;133(4):845-852.
22. Yurdakok M, Ozek E. Transient tachypnea of the newborn: the treatment strategies. Curr Pharm Des 2012;18(21):3046-3049.
23. Kasap B, Duman N, Ozer E, Tatli M, Kumral A, Ozkan H. Transient tachypnea of the newborn: predictive factor for prolonged tachypnea. Pediatr Int 2008;50(1):81-84.
24. Malakian A, Dehdashtian M, Aramesh MR, Aletayeb MH, Heidari S. The effect of inhaled salbutamol on the outcomes of transient tachypnea of the newborn. J Chin Med Assoc 2018;81(11):990-997.
25. Kao B, Stewart de Ramirez SA, Belfort MB, Hansen A. Inhaled epinephrine for the treatment of transient tachypnea of the newborn. J Perinatol 2008;28(3):205-210.
26. Davies JC. Ion transport in lung disease. Pediatr Pulmonol Suppl 2004;26:147-148.
27. Alhassen Z, Vali P, Guglani L, Lakshminrusimha S, Ryan RM. Recent advances in pathophysiology and management of transient tachypnea of newborn. J Perinatol 2021;41(1):6-16.
28. Broadley KJ. Beta-adrenoceptor responses of the airways: for better or worse? Eur J Pharmacol 2006;533(1-3):15-27.
29. Nicklas RA. Paradoxical bronchospasm associated with the use of inhaled beta agonists. J Allergy Clin Immunol 1990;85(5):959-964.