

Intravenous Furosemide in the Management of Transient Tachypnea of Newborn

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ABSTRACT

Objective: To determine the mean length of hospital stay of term and late preterm infants with transient tachypnea of the newborn treated with intravenous Furosemide compared to the Control Group.

Study Design: Quasi-experimental study.

Place and Duration of Study: Combined Military Hospital, Kharian, from Apr to Oct 2016.

Methodology: All term and late preterm infants with transient tachypnea of new-borns were included in the study. One Group was given IV Furosemide, and the other was taken as control. Two doses of Furosemide were administered IV at 1 mg/kg 12 hours apart. The Control Group were given normal saline 01 ml/kg as a placebo 12 hours apart.

Results: It was found that the duration of tachypnea in the Study-Group was less than that of the Control-Group (49.4 ± 7.4 h vs 76.7 ± 4.5 h, p -value < 0.001). The requirement of oxygen was less in the Treatment Group (53.7 ± 6.6 h) as compared to the Control-Group (84.5 ± 4.2 h) ($p < 0.01$). The duration of hospitalization in the Study-Group was 71.4 ± 4.9 hours, and in the Control-Group was 100.0 ± 3.7 hours (p -value < 0.001).

Conclusion: Using intravenous Furosemide in neonates with transient tachypnea of newborns effectively reduces the hospital stay of term and late preterm patients. It reduced the tachypnea and, subsequently, the requirement for oxygen in patients with transient tachypnea in newborns.

Keywords: Furosemide, Hospital stay, Transient tachypnea of newborn, Term and late preterm newborns.

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INTRODUCTION

Transient tachypnea of the newborn (TTN) is one of the common causes of respiratory distress in the early neonatal period. TTN is caused by the delayed resorption of fluid from the alveoli of the fetal lungs.¹ The incidence of TTN is 5.7 per 1000 births out of 33,289 term deliveries (37 to 42 weeks).² There is an increased risk of transient tachypnea of the newborn after cesarean section compared to vaginal delivery. There is no protective role of labour induction before cesarean delivery.^{3,4}

Physical findings in TTN include increased respiration, grunting, flaring, and chest retractions. Most patients have only an increased rate of respiration.⁵ In extreme cases, there may exhibit severe hypoxia and cyanosis. It is found that a respiratory rate greater than 90 breaths per minute during the first 36 hours of life is associated with prolonged tachypnea, which lasts for more than 72 hours. 5TTN is caused by increased airways liquid volumes resulting in decreased respiratory function.⁶ The longer duration of TTN is supposed to be caused by reduced synthesis of nitric oxide in the lungs.⁷ Pregnancy-induced hypertension is a risk

factor for developing TTN.⁸ Neonatal transport adversely affects newborns and may lead to TTN.⁹ Ultrasound of the lungs can diagnose TTN based on findings of pulmonary oedema, white lung and alveolar interstitial syndrome.¹⁰

The rationale of the study was to see the clinical effect of intravenous Furosemide in patients with TTN since limited studies are available on the intravenous use of Furosemide in TTN. Hence in countries like Pakistan, where there are limited resources and more patient burden in neonatal ICU, intravenous Furosemide could be advised to patients to reduce their hospital stay in neonatal ICU.

METHODOLOGY

The quasi-experimental study was carried out at the Neonatal Intensive Care Unit of Combined Military Hospital Kharian, after approval of the Ethical Review Board from April to October 2016. The sample size was calculated using the WHO sample size calculator taking, population mean 106.08 ± 37 and population mean 125.7 ± 46.3 .¹¹

Inclusion Criteria: All term and late preterm infants with a diagnosis of TTN of either gender were included in the study.

Exclusion Criteria: Patients having respiratory distress other than TTN were excluded from the study.

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The sample size was 200, 100 patients each in Control and Study Groups. The sampling technique was Consecutive (Non-probability) sampling. They were diagnosed based on physical examination, chest X-rays, blood CP, BSR, CRP and blood cultures. These included babies with Meconium aspiration (meconium stained cord and skin, lung opacities and hyperinflation of lungs on chest x-rays), Neonatal Respiratory Distress Syndrome (Air bronchogram on chest x-rays), Pneumonia (consolidation on chest x-rays), Early-Onset Neonatal Sepsis (positive CRP and blood culture), Polycythemia or Hypoglycemia (Hematocrit greater than 60% and BSR less than 54 mg/dl respectively), Heart Murmur (audible on auscultation) and Tachycardia (heart rate greater than 180/min). The purpose and benefits of the study were explained to the parents of the patients. They were assured of the purpose and benefits of the study and the risk involved, and they were explained that the study was done purely for research and data publication. When agreed upon, written consent was taken from the parents of the study.

All patients were subjected to detailed history and clinical exams. The concerned experienced pathologist with a minimum of 5 years of experience reported all the laboratory investigations. All patients with TTN were divided into two groups by lottery method. One Group was given IV Furosemide, and the other was taken as control. Two doses of Furosemide were administered IV at 1mg/kg 12 hours apart. The Control-Group were given normal saline 01ml/kg as a placebo 12 hours apart. The rest of the treatment was kept uniform for all patients per NICU guidelines and was decided by a single expert Paediatrician with a minimum of 05 years of experience. All patients were followed after initiation of treatment to determine the effectiveness of therapy. All the information, was recorded as per the designed proforma.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Mean \pm SD were calculated for quantitative variables. Hospital stay between the two groups was compared by independent sample t-test. The *p*-value of ≤ 0.05 was set as the cut-off value for significance.

RESULTS

The study included two hundred infants, 100 in the Treatment Group (intravenous Furosemide); and 100 in the Control Group (intravenous saline). The average gestational age was found to be 38.25 \pm 1.977 weeks, and the average birth weight was 2.8232 \pm

0.43268kg. About 76 babies were born through cesarean section, 71 through emergency cesarean section and 56 through spontaneous vaginal delivery, as given in Table-I.

Table-I: Demographic Characteristics (n=200)

Variables	Treatment-Group (100)	Control-Group (100)
Male	64(64%)	64(64%)
Female	36(36%)	36(36%)
Term gestation	74(74%)	70(70%)
Late preterm gestation	26(26%)	30(30%)
Average birth weight (kg)	2.8 \pm 0.4	2.7 \pm 0.4
Average onset of onset of Tachypnea (hours)	2.0 \pm 0.5	1.9 \pm 0.4
Type of Delivery		
Elective C-section	36(36%)	37(37%)
Emergency c section	34(34%)	37(37%)
Vaginal delivery	30(30%)	26(26%)

It was found that the onset of tachypnea was at 2.0 \pm 0.5 hours in cases and at 1.9 \pm 0.4 hours in Control Groups. The duration of tachypnea in cases was 49.4 \pm 7.4 hours after intravenous Furosemide, which was shorter than the duration of tachypnea in the Treatment Group (76.7 \pm 4.5h, respectively); the difference was significant (*p*<0.05). The difference between oxygen requirement in the Treatment-Group versus Control-Group was also significant (53.7 \pm 6.6h vs 84.5 \pm 4.2h) (*p*<0.01). The duration of hospitalization in the Study Group was 71.4 \pm 4.9 hours, and in the Control Group was 100.0 \pm 3.7hours with a *p*-value <0.001 as given in Table-II.

Table-II: Efficacy of Furosemide (n=200)

Variables	Treatment-Group (100)	Control-Group (100)	<i>p</i> -value
Period of Tachypnea (in hours)	49.4 \pm 7.4	76.7 \pm 4.5	<0.001
Period of Oxygen Requirement (in hours)	53.7 \pm 6.6	84.5 \pm 4.2	<0.001
Period of Hospitalization (in hours)	71.4 \pm 4.9 69.2 \pm 3.5 (n=74)	100.0 \pm 3.7 98.2 \pm 2.4 (n=70)	<0.001
Term babies	77.6 \pm 2.2 (n=26)	104.3 \pm 2.8 (n=30)	
Late preterm	71.12 \pm 5.0 (n=64)	100.4 \pm 3.7 (n=64)	
Male babies	72.0 \pm 4.9 (n=36)	99.6 \pm 3.8 (n=36)	

DISCUSSION

A newborn with TTN has an increased risk of respiratory syncytial virus bronchiolitis infection in the first year of life. General management of TTN includes supplemental oxygen delivered through a head box or continuous positive airway pressure, withholding enteral feeding until the respiratory distress resolves, intravenous maintenance fluids and antibiotics.^{11,12} Some of the treatment strategies that may be helpful include Furosemide, racemic epinephrine and inhaled beta-agonists. The routine administration of these treatments cannot be recommended due to limited data.¹³ Studies are needed to evaluate the effect of corticosteroids in managing TTN. TTN be reduced by applying prophylactic CPAP. There is no benefit of inhaled corticosteroid in the clinical course of TTN.^{13,14}

Karabayer *et al.* in 2006, randomized 50 infants with TTN to receive IV Furosemide. Results showed that the duration of hospitalization of patients with TTN was 106.08 ± 37.1 hours in the Study Group compared to 125.2 ± 46.3 hours in the Control Group with a *p*-value of 0.122.¹⁵ A study carried out by Wiswell *et al.* on oral use of Furosemide has not shown any benefit in either the severity or duration of the illness or length of hospitalization.¹⁶ In addition, oxygen supplementation was reduced in those patients with restricted fluids compared to standard fluid therapy.¹⁷ Moresco *et al.* compared different treatment modalities for TTN like inhaled epinephrine and salbutamol, fluid restriction, non-invasive ventilation and Furosemide and found that hospital stays for the Salbutamol Group were significantly shorter than other interventions.¹⁸

The main aim of our study was to observe the effect of IV Furosemide on the length of hospital stay in patients with TTN compared with the Control Group. At the end of the study, we compared the duration of tachypnea, oxygen requirement, and duration of hospitalization between cases and the Control Group. Both groups had similar birth and maternal events that could have affected the clinical symptoms. These findings suggest that intravenous Furosemide therapy may be useful in treating transient tachypnea in newborns. There was no tachycardia, dehydration or any significant side effect with Furosemide in the Group. TTN tends to resolve spontaneously, but with IV Furosemide, the duration of tachypnea and the requirement of oxygen needed was shorter in patients treated with intravenous Furosemide compared to the Control Group. Similarly, hospital stay is shorter in the

Treatment Group than in the Control Group. In our study, the duration of hospitalization is reduced by almost 29 hours with *p*-value < 0.01 . This was significant as in countries with limited resources and more patient burden in neonatal ICUs, more beds will be available for sick and serious patients with other diseases. However Further studies are required to see the effects of IV Furosemide on TTN and validate our findings.

CONCLUSION

We conclude through our study that intravenous Furosemide has a role in the early resolution of tachypnea, reduction in oxygen requirement and ultimately, reduction of hospital stay in patients with TTN.

Conflict of Interest: None.

Authors Contribution

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

SA & AR: Conception, study design, data interpretation, approval of the final version to be published.

SAS: Data acquisition, data analysis, drafting the manuscript, approval of the final version to be published.

ZA: Critical review, interpretation of data, 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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