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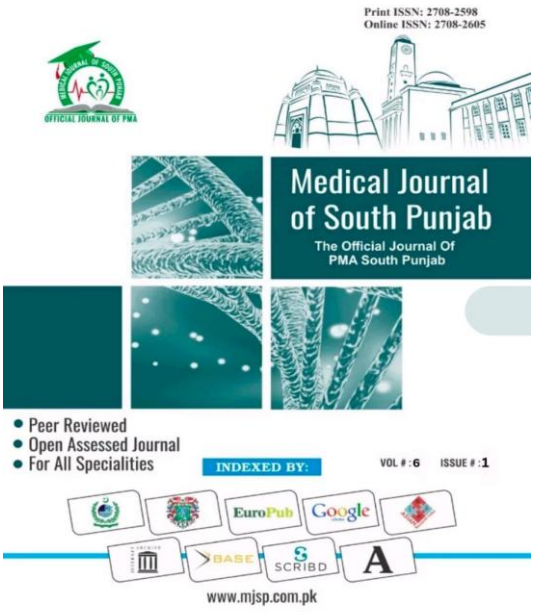

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Original Article

Efficacy Of Furosemide in the Management of Transient Tachypnoea of Newborn

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ABSTRACT

Objective: To see the efficacy of intravenous Furosemide in the management of transient tachypnoea of newborn.

Methods: This study was conducted at the Department of Paediatrics, Fauji Foundation Hospital Rawalpindi from August to December 2024**.** Neonates with 34 to 40 weeks of gestation diagnosed with TTN and requiring CPAP to maintain oxygen saturation > 90% were included. Neonates born with congenital malformations, systemic infection, requiring mechanical ventilation and intubation were excluded. Intravenous furosemide was administered to Group A, while Group B was managed conservatively and normal saline as a placebo was used. Following the start of therapy each patient will be monitored to assess the efficacy of the therapy, in terms of length of hospital stay and duration of oxygen therapy.

Results: One hundred and seventy-two (n=172) patients had a mean gestational age of 38.45±1.07 weeks. The respiratory rate at admission was 84.75±15.49 breaths/minute in Group A and 82.69±13.89 breaths/minute in Group B with no statistical difference (p=0.403). Post-intervention in Group A the respiratory rate was 46.61±4.97 breaths/minute and in Group B it was 51.24±4.27 breaths/minute (p<0.001). The control group required longer mean oxygen therapy than the Furosemide group. Similarly, the mean length of hospital stay was also higher in Group B than in Group A (p<0.001).

Conclusion: The treatment with furosemide significantly improved the transient tachypnoea of newborns but it also decreased the duration of oxygen therapy and length of hospital stay.

Keywords: Continuous Positive Airway Pressure, Furosemide**,** Oxygen inhalation therapy, Transient Tachypnea of the Newborn.

1. INTRODUCTION

Transient tachypnoea of the newborn (TTN), another name for respiratory distress from retained fetal lung fluid, can occur when a newborn is unable to effectively clear the fluid from their lungs soon after birth..1 The incidence of TTN is as high as 16 newborns per 1000 births, a large number requiring not only immediate emergency care but also raising the need to do research in the subject field.2 The higher incidence was seen in males, term births and babies born through lower section cesarean section. TTN is a benign-looking ailment that settles in 2 to 3 days after birth spontaneously. It has long-lasting impacts in the form of high-dependency infant oxygenation, medical care and prolonged exposure to medications right after the birth posing a risk to other organs like kidneys and liver.3 Moreover, it also has psychological implications on the mother in the form of maternal-infant separation. TTN was found associated with different respiratory syndromes including asthma in younger and adult stages of life. [4]

Early diagnosis of TTN is essential for appropriate treatment and avoiding the disease's complications. Furosemide is a loop diuretic that is responsible for excreting water secretion and has been identified to regulate fluid dynamics in diuretic and non-diuretic conditions and is responsible for accelerating lung fluid clearance. Various modalities have been used and developed to manage TTN, including the ultrasonography of the lungs which shows b-lines, similarly continuous positive airway pressure (CPAP) has been used to decrease the respiratory effort and maintain adequate levels of oxygen saturation.[1,5] It has been postulated that the rapid clearance of fluid retained in the lungs can improve oxygenation and reduce disease morbidity.[6] It has been determined that furosemide may alter the clinical results of TTN based on its known effect on fluid overload lung. Furosemide is fast-acting and has shown efficacy in neonates and adults. Its use is beneficial in clinical conditions that require high diuretic potential.[7] A study showed a positive impact of intravenous Furosemide in patients of transient tachypnoea of newborns in terms of decreased oxygen requirement and hospital stay.[8] Another study demonstrated the beneficial effects of furosemide and salbutamol in the treatment TTN.[9]

The rationale for researching the efficacy of intravenous Furosemide in the management of transient tachypnoea of the newborn (TTN) stems from the need to optimize therapeutic strategies and improve outcomes for neonates afflicted by this condition. To our knowledge, there is limited research on the efficacy of Furosemide in managing TTN within the context of Pakistan's healthcare landscape. Our present study aims to bridge this gap by providing valuable insights into the utility of Furosemide as an adjunct therapy for TTN in Pakistani neonates. By conducting a randomized control trial involving neonatal intensive care units (NICUs) across Pakistan. we seek to generate evidence that is directly applicable to local clinical practice.

2. METHODOLOGY

This randomized control trial was carried out at the Department of Obstetrics and Gynaecology, and Paediatrics, Fauji Foundation Hospital Rawalpindi. The study was started after approval from the Institutional Ethical Approval Committee vide certificate number: 853/RC/FFH/RWP. The sample size was calculated using an OpenEpi Sample Size Calculator with a significance level of 95%, power of 80% and population mean of 106.08+37.0 for Group A and 125.70+46.30 for Group B, the sample size came out to be 144 newborns with 72 babies in each group.[10] The informed written consent was taken from guardians, next of kin (NOK)

and parents of all newborns as applicable. The non-probability consecutive sampling technique was used to enrol participants. Neonates with 34 to 40 weeks of gestation diagnosed with TTN and requiring CPAP to maintain oxygen saturation > 90% were included in the study. Neonates born with congenital malformations, systemic infection, requiring mechanical ventilation and intubation were excluded. Moreover, neonates having acute respiratory distress syndrome (ARDS), suspected meconium aspiration and congenital pneumonia, and those receiving cardiopulmonary treatment with support were also excluded.

By using a lottery, all TTN patients were split up into two groups with 72 patients in each group. IV furosemide was administered to Group A, while Group B was managed conservatively and normal saline as a placebo was used. After a detailed history and a clinical examination, the intravenous furosemide at the rate of 1mg/kg will be given at an interval of 12 hours to Group A while a placebo of normal saline at the rate of 0.1ml/kg will be administered to Group B at similar intervals. According to neonatal intensive care unit (NICU) principles, the remaining level of care will be kept consistent for every patient and will be determined by a single, highly skilled paediatrician with at least five years of experience. The blinding will be done for the treating paediatrician and NICU nurses. The blinding will be achieved through the allocation of a random sequence of numbers. Following the start of therapy each patient will be monitored to assess the efficacy of the therapy, in terms of length of hospital stay and duration of oxygen therapy. Complications in terms of vomiting, allergic response or any other will be measured and mortality will be noted. Every piece of information will be documented using the pre-made proforma.

Data will be collected, entered and analysed using Statistical Package for Social Sciences (SPSS) version 25.0. The normality of quantitative variables will be checked by using the Shapiro-Wilk Test. Mean or median and Standard Deviation (SD) or interquartile range (IQR) will be measured for quantitative variables as per the results of the Shapiro-Wilk test. Frequencies and percentages will be calculated for qualitative variables. The independent Sample T-test will used to test the statistical association between the groups. The p-value < 0.05 will be considered as statistically significant.

3. RESULTS

There were one hundred forty-four (n=144) newborns, with seventy-two babies in each group. The mean gestational age of the participants was 38.45±1.07 weeks. The mean weight of newborns was 3.04±0.31 kgs, while the mean respiratory rate at the time of admission was 83.72±14.70 breaths/minute. The mean length of hospital stay was 62.40±14.90 hours. The mean oxygen therapy time was 58.46±12.84 hours. The details are given in Table-I.

Table-I: Baseline characteristics of sample populations (n=144)

Variables	Intervention Groups		p-value
	Group-A	Group-B	
Gestational Age	38.40±1.12	38.50±1.03	0.590
Gender • Male • Female	 37 (51.39%) 35 (48.61%)	 42 (58.33%) 30 (41.67%)	0.402
Weight	3.04±0.32	3.03±0.31	0.832
Mode of Delivery • Vaginal Delivery • LSCS	 29 (40.28%) 43 (59.72%)	 24 (33.33%) 48 (66.67%)	0.388
Maternal Asthma • Yes • No	 14 (19.44%) 58 (80.56%)	 13 (18.06%) 59 (81.94%)	0.831

The respiratory rate at admission was 84.75±15.49 breaths/minute in Group A while 82.69±13.89 breaths/minute in Group B with

no statistical difference (p=0.403). Post-intervention in Group A the respiratory rate was 46.61±4.97 breaths/minute, on the other hand in Group B it was 51.24±4.27 breaths/minute and the results were statistically significant (p<0.001). The control group (Group B) required longer mean oxygen therapy 67.68±9.45 hours than the Furosemide group (group A) 49.25±8.41 hours. Similarly, the mean length of hospital stay was also higher (71.22±15.22 hours) in Group B than in Group A (53.58±7.59 hours). The difference was statistically significant (p<0.001) in terms of mean oxygen therapy and the mean length of hospital stay (Table-II).

Table-II: Comparison of Respiratory rate, oxygen therapy and length of hospital stay between Group A and Group B (n=144)

Variables	Intervention Groups		p-value
	Group-A	Group-B	
Respiratory Rate • Baseline • Post-intervention	 84.75±15.49 46.61±4.97	 82.69±13.89 51.24±4.27	 0.403 <0.001
Oxygen Support	49.25±8.41	67.68±9.45	<0.001
Length of Hospital Stay	53.58±7.59	71.22±15.22	<0.001

Few patients from both groups reported symptoms apart from symptoms of TTN during treatment shown in Table-III. No mortality was reported from either group.

Table-III: Patient outcomes and side effects (n=144)

Outcome	Groups	
	Group A	Group B
Vomiting	3 (4.17%)	2 (2.78%)
Diarrhoea	2 (2.78%)	2 (2.78%)
Hypotension	1 (1.39%)	-
Hypokalaemia	1 (1.39%)	-

4. DISCUSSION

The TTN is one of the respiratory distress syndromes with long-term implications like wheezing syndromes and asthma when compared against similar age groups.[11] Recent studies suggest that fluid retention in the lungs is not only associated phenomenon associated with TTN but higher fluid volumes are present at birth too, causing the seepage of fluid into airways.[12,13] In this study, one hundred and forty-four newborns were enrolled. Group A (Furosemide group) had better patient outcomes when compared with Group B (Control group). Both the groups had no statistically significant difference in baseline parameters like gestational age, birth weight, baseline respiratory rate, gender, mode of delivery and maternal asthma history. However, Group A had better outcomes with comparatively lower respiratory rate (P<0.001) and lesser duration of hospital stay. The duration of oxygen therapy in Group A was also lesser than the Group B with a mean difference of 18.43±1.04 hours.

In a similar study by Ali et al done in Pakistan in a tertiary care hospital, they found Furosemide was effective in TTN.[14] It not only reduced the hospital stay, and the respiratory rate but also improved the oxygen requirement of the newborns with TTN. In this study too, hospital stay was shorter in the Furosemide group, and the tachypnoea improved compared to the placebo group similarly oxygen requirement was less in the Furosemide group in contrast to the control group. In many recent studies, the role of diuretics has been studied.[15,16] This reflects the role of diuretics like Furosemide in the management of transient tachypnoea which work by causing increased urinary excretion fluids via normal physiological pathways.

In another randomized control trial, the researchers studied the effects of Salbutamol and intravenous Furosemide and found promising results with combination

therapy, though the TTN parameters improved in individual groups but the results were not statistically significant.[17] In this study, a similar effect was observed in individual groups but it was statistically significant. A study by Khushdil et al in Pakistan concluded Furosemide has a beneficial effect on TTN but salbutamol and Furosemide combined have a significant impact.[9] In our study, we made a comparison with a placebo not with Salbutamol but we saw a significant impact of Furosemide therapy in improving respiratory rate and oxygen requirement.

In contrast, a Cochrane review was done on the role of Furosemide in TTN which included two studies. The review summarised that Furosemide had no promising effect on TTN, neither intravenous nor oral, and suggested further investigations and RCTs to see the effect of Furosemide on TTN.[18] In contrast, our study showed a hopeful effect of Furosemide, a loop diuretic, in the management of TTN not only for Tachypnea but also for a mean hospital stay. The mean hospital stay, duration of oxygen therapy and tachypnoea improved in the Furosemide group when compared with the placebo group.

There are certain limitations in our study. Firstly, it has a small sample size and has shorter duration of observation, no long-term effects were seen. There is also an inherent bias of this hospital being a tertiary care setting, where usually complicated cases are seen and managed. Therefore, we suggest a large multicentre clinical trial should be done comparing different treatment modalities and suggesting one more suitable therapy for the management of TTN.

5. CONCLUSION

Furosemide therapy in newborns diagnosed with transient tachypnoea showed promising improvement in respiratory rate, oxygen requirement duration, and mean hospital stay duration compared with placebo. This study highlights the role of diuretics in TTN management and raises the need for further research into this subject.

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