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Comparison of Effects of Salbutamol Inhalation with Continuous Positive Airway Pressure and Bubble Continuous Positive Airway Pressure Alone in the Management of Severe Transient Tachypnea of the Newborn

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ABSTRACT

Objective: To find the frequency of known risk factors in cases of severe transient tachypnea of the newborn (TTN) and to measure the effect of inhaled Salbutamol to bubble CPAP on required treatment duration.

Study Design: Quasi-experimental study.

Place and Duration of Study: Neonatal Intensive Care Unit, Combined Military Hospital, Malir Cantt, Karachi Pakistan, from Nov 2019 to Jun 2020.

Methodology: A total of 60 cases of severe TTN, labelled on a predefined criterion were included in the study. The sample was randomized into two groups using an alternate sampling technique. Group-A was treated with bubble CPAP alone, while in Group-B, inhaled Salbutamol was added. The response was measured regarding the time taken to settle respiratory distress.

Results: Out of 60 cases, 54(90.0%) were delivered through Caesarean section. A total of 9(15.0%) cases were born prematurely. Polycythemia was found in 10(16.6%) cases. Maternal asthma and gestational diabetes frequency were 8(13.33%) and 12(20.0%), respectively. A significant reduction was seen in the duration of respiratory distress in the study population receiving bubble CPAP with inhaled Salbutamol in the first 24 hours of illness (p-value<0.001).

Conclusion: Caesarean section is the most significant risk factor for developing TTN. Adding Salbutamol nebulization to bubble CPAP resulted in an earlier settlement of respiratory distress.

Keywords: Bubble CPAP, Inhaled salbutamol, Risk factors, Transient tachypnea of the newborn.

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INTRODUCTION

Transient tachypnea of the newborn (TTN) is a clinical syndrome of self-limiting tachypnea which appears shortly after birth and is associated with delayed clearance of fetal lung fluid.[1] It usually resolves within the first three days. TTN is diagnosed after excluding all other causes of respiratory distress in newborns. The incidence of TTN is 3.6-5.7/1000 live births and is the commonest cause of respiratory distress in newborns.[2] Various risk factors promoting TTN have been identified. Maternal risk factors include late preterm labour, Caesarean section without preceding labour, maternal diabetes and maternal asthma. Neonatal risk factors include male gender, perinatal asphyxia and small or large for gestational age newborns.[3,4]

Various modalities and pharmaceutical agents have been tried to treat severe TTN. Among these are nasal continuous positive airway pressure (CPAP) which has been proven a safe and useful remedy in various studies and is now recommended for the management of TTN.[5,6] Among pharmaceutical agents, inhaled corticosteroids, oral and injectable Furosemide and Epinephrine, have been tried. However, none of them was found effective and consequently could not be recommended as a standard therapeutic agent for the treatment of TTN so far.[7,8] Inhaled Salbutamol has been found beneficial in some studies nine but ineffective in others.[9,10] Unfortunately, most of these studies were done with inadequate sample sizes, so their results cannot be generalized and more studies are required to conclude. This situation led us to plan a study to compare the response of nasal CPAP alone and in combination with inhaled Salbutamol to treat severe TTN. The objectives of our study were to determine the prevalence of various identified maternal and fetal risk factors for TTN in the study population and to measure the effect of adding inhaled Salbutamol bubble CPAP on the required treatment duration.

METHODOLOGY

This quasi-experimental study was conducted at the Neonatal Intensive Care Unit of Combined Military Hospital Malir Cantt Karachi for eight

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months, from November 2019 to June 2020. Before conducting the study, approval was taken from the Institutional Ethical Review Board. (ERC number 1440/2019/Trg/Adm dated 31 Jan 2020).

Inclusion Criteria: Neonates of either gender, with severe TTN were included in the study, using a consecutive sampling technique.

Exclusion Criteria: Neonates with other causes of respiratory distress in newborns were excluded from the study.

Written consent was taken from the parents of enrolled patients. Diagnosis of severe TTN was made based on having a respiratory rate of >60/min with signs of respiratory distress like grunting, nasal flaring, intercostal, subcostal or suprasternal recess-ions or presence of cyanosis and oxygen saturation of less than 90% checked through a pulse oximeter. Before labelling them a case of TTN, other causes of respiratory distress, including congenital cardiac defects, respiratory distress syndrome, metabolic derangements, persistent pulmonary hypertension, neonatal sepsis, hypothermia and major causes of respiratory distress, were ruled out based on either absence of relevant clinical findings like a cardiac murmur, fits, low body temperature or by carrying out required necessary investigations like x-ray chest, arterial blood gas analysis, blood culture, serum C-reactive protein, serum electrolytes, renal function tests and blood sugar levels. Frequencies and percentages of the selected known risk factors for TTN (gestational age at birth, mode of delivery, birth weight, neonatal polycythemia, maternal asthma and gestational diabetes) in the study population were calculated. As a routine protocol of our nursery, severe TTN is treated with bubble CPAP. In half of the cases, Group-A (randomized on an alternate case basis) was given bubble CPAP alone through nasal prongs. While the other half (Group-B) was given bubble CPAP along with nebulization with aerosol Salbutamol using an ultrasonic nebulizer as per standard protocol. (0.1ml/kg of Salbutamol+2.5ml normal saline nebulized for 10 min every 8 hours). The same nebulizer was used for all the patients of study Group-B. Antibiotics were not given to both study groups since there was no evidence of infection, and unnecessary blood sampling and vigorous handling were avoided. Treatment was continued till achievement of the response, which was labelled as settlement of tachypnea (respiratory rate <60/min) with the absence of the signs as mentioned earlier of respiratory distress, oxygen saturation of >94% checked with pulse oximeter at room air and the patient taking and tolerating oral feed. Other than slight tachycardia (heart rate 160-170 beats/min), no significant adverse effects of Salbutamol were observed in treatment Group -B. Oxygen supply was kept the same for all cases (40%) during the treatment. Data were recorded on predesigned Performa containing variables regarding risk factors for TTN and response to the given therapy, measured in terms of hours duration for which therapy was continued for settlement of tachypnea.

Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Quantitative variables were summarized as Mean±SD and qualitative variables were summarized as frequency and percentages. Independent sample t-test was applied to find the mean differences among the groups. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

Sixty cases of severe transient tachypnea of newborns (TTN) were enrolled. Of them, 31(52.0%) were male newborns, and 29(48.0%) were female newborns. A total of 9 newborns (15.0%) were delivered preterm (<37 weeks of gestation), 43(71.6%) were born full term (37-40 weeks of gestation), and 8(13.3%) were born at more than 40 weeks of gestation. Polycythemia, was seen in 10 newborns (16.6%).

A notable finding was that 54(90%) newborns were delivered through Caesarean section. The study sample was divided into two groups. Group-A was treated with only bubble CPAP, while Group-B was given bubble CPAP and Salbutamol nebulization according to standard protocol. In both groups, treatment continued until the achievement of response as per the above-mentioned criteria. Their response in terms of required treatment hours duration has been shown in Table-I. In both groups, an almost similar response pattern was noted. However, comparing the number of cases in which TTN was resolved with treatment duration of 4-6hours, 6-12 hours and 12-24 hours, at a 95% confidence interval, (*p*-value of<0.01).

Table-I: Duration of Settlement of Tachypnea of the Newborn in the Study Groups (n=60)

Duration of Settlement of Tachypnea	Group-A (n=30) (Mean±SD)	Group-B (n=30) (Mean±SD)	*p*-value
4-6 hours	3.97±1.178	4.02±1.172	<0.01
6-12 hours	3.97±1.178	4.02±1.172	<0.01
12-24 hours	3.97±1.178	4.02±1.172	<0..01
24-36 hours	3.97±1.178	4.02±1.172	0.827

A history of gestational diabetes was found in,[12] cases (20.0%), while eight mothers (13.3%) of the study population were asthmatic. The mode of delivery, birth weight and gestational age of the study population has been shown in Table-II.

Table-II: Mode of delivery, Birth Weight and Gestational Age in the Study Groups (n=60)

	Mode of Delivery			Birth Weight				Gestational Age		
	Spontaneous vaginal delivery	Emergency lower segment cesarean section	Elective lower segment cesarean section	2-2.5 kg	2.5-3 kg	3-3.5 Kg	>3.5 Kg	<37 Wks.	37-42 Wks.	>42 Wks.
Group -A(n=30)	5(16.7%)	10(33.3%)	15(50.0%)	2 (6.6%)	12 (40.2%)	14 (46.6%)	2 (6.6%)	3 (10.0%)	23 (76.7%)	4 (13.3%)
Group -B(n=30)	3(10.0%)	10(33.3%)	17(56.7%)	2 (6.6%)	14 (46.8%)	10 (33.3%)	4 (13.3%)	5 (16.6%)	21 (70.1%)	4 (13.3%)

DISCUSSION

The focus of our study was on the frequency of previously identified risk factors for TTN in our study population and the comparison of responses to the two different therapies given to them. The results of our study were comparable to the previous studies on this subject. Maternal risk factors included in our study were the presence of gestational diabetes and maternal asthma. In contrast, fetal risk factors included gestational age at birth, delivery mode, and polycythemia. TTN is more common in male neonates; however, in our study population, both genders were almost equally affected (31 males and 29 females).

Similarly, the risk of developing TTN is inversely proportional to the gestational age, decreasing with advancing gestational age.[11,12] In our study, only 15% of the newborns were premature, while 71% were full-term neonates. Elective cesarean section was a common risk factor found in our study (found in 56% of the study population) and those done by Zuhal *et al.* and Hamdoon *et al.* where 67% and 56% study cases were delivered through elective cesarean section respectively.[13,14]

Polycythemia was found only in 16.6% in our study, while in Mostefa *et al.* study, 24.87% of polycythemic neonates developed TTN.[15]

A significant finding of our study was the detection of the significant advantage of adding Salbutamol nebulization to CPAP therapy for early control of respiratory distress in TTN. In both study groups, tachypnea settled mostly within 12-24 hours of starting therapy. The number of treated cases in each treatment duration section was also comparable. The addition of Salbutamol nebulization failed to reduce the duration of respiratory distress. One such variable might be COVID-19 since the study was conducted during the COVID-19 pandemic, and we could not screen every participant for coronavirus. The other reason could be an inadequate sample size. Surprisingly, statistics regarding response to 24-36 hours of therapy revealed opposite results with a *p*-value of 0.8, which denoted that if bubble CPAP therapy is needed for more than 24 hours, then inhaled Salbutamol does not significantly confer any added benefit. This impression necessitates and suggests further research and evaluation. The role of Salbutamol in treating TTN has been assessed in previous studies with inconclusive evidence.[16-18]

LIMITATIONS OF STUDY

This study was conducted during the COVID-19 pandemic when the hospital burden for general patients was less than the regular turnover. Therefore, we could not find a large sample size as it should provide conclusive evidence. Furthermore, since our study population comprised cases of severe TTN so we had to combine Salbutamol nebulization with bubble CPAP therapy. For a better understanding of the role of Salbutamol in TTN, it should be assessed as a sole therapy in different grades of TTN.

CONCLUSION

Most of the study population of severe TTN was born full-term and delivered through cesarean section. A significant difference was observed in time taken for settlement of tachypnea with adding Salbutamol nebulization to bubble CPAP therapy in the first 24 hours of treatment, while if treatment is needed for more than 24 hours, the addition of inhaled Salbutamol does not provide any significant benefit.

Conflict of Interest: None.

Authors' Contribution

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

WA & STHZ: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

AS & WS: Conception, Study design, drafting the manuscript, approval of the final version to be published.

BF & AM: Data interpretation, critical review, 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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