Open Access

Original Article

Early Complications of Surfactant Administration In Neonates

Hafiz Zulqarnain, Muhammad Tariq Nadeem, Sammar Hussain, Ali Mujtaba*, Saeed Zaman, Waleed Ali

Department of Pediatrics, Pak Emirates Military Hospital /National University of Medical Sciences (NUMS) Rawalpindi Pakistan,
*Department of Pediatrics, Combined Military Hospital Zhob /National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To assess the early complications of surfactant administration in neonates with respiratory distress syndrome.
Study Design: Perspective longitudinal study.
Place and Duration of Study: Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan, from Jun to Dec 2021.
Methodology: A total of 64 neonates admitted in ICU with gestational age 27-32 weeks requiring Continuous Positive Airway Pressure and surfactant administration were included. Neonatal complications after 24 hours of administration of surfactant and final outcome was recorded on a predesigned data collection tool.
Results: Mean duration of stay on ventilator was 41.12±8.88 hours. Mean duration for Continuous Positive Airway Pressure was 43.59±22.70 hours. Second dose of surfactant was given to 34(53.1%) of neonates. Among neonates 25% suffered from pulmonary hemorrhage and 7.8% from bradycardia, 48(75%) were discharged and 16(25%) died.
Conclusion: The mortality rate decreased in neonates after administration of surfactant. In future, we will implement surfactant in term neonates, diagnosed with Respiratory Distress Syndrome, in order to improve the survival of neonates and reduce complications.

Keywords: Bradycardia, Complications, Neonates, Surfactant, Pulmonary hemorrhage.

How to Cite This Article: *Zulqarnain H, Nadeem MT, Hussain S, Mujtaba A, Zaman S, Ali W. Early Complications of Surfactant Administration In Neonates. Pak Armed Forces Med J 2024; 74(3): 821-824. DOI: https://doi.org/10.51253/pafmj.v74i3. 8675*

INTRODUCTION

Respiratory morbidity affects 15% of term babies and 29% of late preterm infants admitted to the neonatal critical care unit; this figure is significantly greater for children born before 34 weeks' gestation.[1] Respiratory distress syndrome (RDS) can occur in premature infants as a result of surfactant deficiency and under-developed lung anatomy.[2] Ventilator therapy with various modes such as Continuous Positive Airway Pressure (CPAP), conventional mechanical ventilation, ultra-high frequency jet ventilation, liquid ventilation, surfactant replacement therapy, sophisticated monitoring, and extracorporeal membrane oxygenation have all improved the outcome of patients with respiratory distress.[3] The development of surfactant replacement therapy for the treatment of respiratory distress syndrome remains one of the most significant advancements.[4] Surfactant treatment improves preterm neonatal respiratory state, reduces ventilator need, hospitalization rates, and improves overall outcome.[5] Medical treatment of very preterm newborns has relied heavily on surfactant replacement therapy. RDS is treated or prevented in most newborns of this gestational age group with surfactant treatment.[6] Surfactants, whether of animal or synthetic origin, have been shown to decrease infant mortality by 40%.[7] The standard therapy for RDS is the administration of an exogenous surfactant. Many studies have shown that administering surfactant prophylactically has advantages over late "rescue" treatment.[8] Premature infants at risk of RDS frequently get prophylactic surfactant in the birth room during their early stabilization, and this has been routine practice for a long time. Endotracheal intubation is needed to deliver the surfactant in this method, making it invasive. It has become clear that there is a need to look into other types of surfactant replacement treatment in light of the potential side effects of surfactant delivery through endotracheal tube such as bradycardia, hypoxia, and hypotension.[9] Over the last decade, randomized controlled trials have enrolled over 2500 infants to compare CPAP versus intubation and intermittent positive pressure ventilation at birth. Unfortunately, these clinical trials reported no differences in the incidence of Bronchopulmonary Dysplasia (BPD) or associated complications of prematurity.[10]

Surfactants are beneficial for management of neonates with RDS, but limited data was reported from our region as no trial done in Pakistan as well.

Correspondence: Dr Hafiz Zulqarnain, Department of Pediatrics, Pak Emirates Military Hospital, Rawalpindi Pakistan
Received: 10 May 2022, revision received: 31 Jul 2023; accepted: 03 Aug 2023

Therefore, we conducted this study to determine the role of surfactant and prevent mortality due to RDS in term neonates and to assess the complications of surfactant administration in neonates with RDS. Neonates were including by applying non-probability purposive sampling technique.

METHODOLOGY

The perspective longitudinal study conducted at Pak Emirates Military Hospital, Rawalpindi from June to December 2021, after approval was obtained from the Institutional Ethical Review Board. Sample size was calculated using Open Epi with incidence of RDS as 15% in term neonates.[1]

Inclusion Criteria: Neonates of either gender, admitted in ICU with gestational age 27-32 weeks, diagnosed with RDS requiring CPAP and surfactant administration were included.

Exclusion Criteria: Neonates with any congenital anomaly and APGAR score <5 were excluded.

All neonates were admitted to Neonatal Intensive Care Unit (NICU). Demographics were noted and parental consent was taken to administer surfactant using Minimally Invasive Surfactant Therapy (MIST) in which the semi-rigid catheter was also removed after administering the entire dose in 5–10 minutes. The CPAP continued to be used for respiratory support. All neonates were followed-up and outcome was noted. Neonatal complications after 24 hours of administration of surfactant and outcome including post-surfactant remained on ventilator (in hours), post surfactant remained on CPAP (in hours), second dose of surfactant administered, pulmonary hemorrhage (detected on chest x-ray), intraventricular hemorrhage (detected on CT scan), bradycardia, tachycardia and stats at discharge (died or alive) were recorded if observed during hospital stay by researcher on data collection tool.

Data analysis was carried out with the help of Statistical Package for the Social Sciences (SPSS) version 23.0. Quantitative variables were presented as mean ± SD and qualitative variables were presented with frequency and percentages.

RESULTS

A total of 64 neonates were included in this study. Mean weight of neonates was 1410.94±193.64 g. Mean gestational age of neonates was 30.04±1.25 weeks. There were 41(64.1%) male neonates and 23(35.9%) female neonates. The male-to-female neonates was 1.8: 1 (Table-I). Mean hours of life at the time of surfactant administration were 30.04±1.2 hours. The mean duration of Post-surfactant ventilator duration was 41.12±8.88 hours. Mean duration for post surfactant CPAP duration was 43.59±22.70 hours. Second dose of surfactant was given to 34(53.1%) neonates. Among neonates 16(25%) suffered from pulmonary hemorrhage, intraventricular hemorrhage was absent (0%) in all cases and 5(7.8%) from bradycardia. Among neonates 48(75%) were discharged alive from hospital and 16(25%) died (Table-II).

Table-I: Descriptive Characteristics Of Neonates At Presentation (N=64)

Characteristics	Mean ± SD
Gestational Age (Weeks)	30.04±1.25
Weight (g)	1410.94±193.64
Gender	n(%)
Male	41(64.1%)
Female	23(35.9%)

Table-II: Outcomes Of Neonates After Treatment With Surfactant (N=64)

Outcomes	n(%)
Need Ventilator (Yes/No)	12(18.8%)
Hours of life at surfactant Administration	12.82±5.88
Post surfactant remained on Ventilator (hours) Mean±SD	41.12±8.88
Post surfactant remained on CPAP (hours) Mean±SD	43.59±22.70
2ND dose of surfactant admin (Yes/No)	34(53.1%)
Pulmonary Hemorrhage	16(25%)
Intraventricular hemorrhage	0(0%)
Bradycardia (heart rate <60 bpm)	5(7.8%)
Tachycardia (heart rate >100 bpm)	0(0%)
Outcome (Discharged / Mortality)	48(75%) / 16(25%)

DISCUSSION

This study aimed to determine the role of surfactant in prevention of mortality due to Respiratory Distress Syndrome in term neonates and to assess the complications of surfactant administration in neonates with RDS. According to literature, neonatal bradycardia and hypotension may result from the use of surfactant as oxygen desaturation has been reported as a side effect of the medication along with tubal delivery of any medication being reported as a significant hazard due to traditional methods of surfactant administration requiring an endotracheal tube.[11] Transient oxygen desaturation and bradycardia may be caused by rapid liquid injection into the lungs, but there are also serious consequences including severe airway

blockage, pulmonary bleeding, pneumothorax, or pulmonary hypertension.[12] Studies also reported that preterm babies with RDS who get surfactant treatment are at an increased risk of developing severe pulmonary bleeding, which has a high fatality rate.[13] Hemorrhage in the lungs has been linked to substantial morbidity and death in prior investigations, with fatality rates ranging from 50% to 82%.[14] As many as 3.2% of very low birth weight babies in Taiwan suffered serious pulmonary bleeding, according to a recent research.[15] Bozkaya *et al*. found a link between pulmonary bleeding and premature baby respiratory morbidities including BPD and extended mechanical ventilation. Infants with pulmonary bleed have a greater risk of additional morbidities including ROP and extended hospitalization.[16] Refractory hypoxemia, acidosis, and inappropriate pulmonary hemorrhage, meconium aspiration syndrome, pneumonia, sepsis, and congenital diaphragm hernia can cause persistent pulmonary hypertension, and surfactant therapy has been proven to be helpful.[17] In our study, pulmonary hemorrhage was noted in 25% cases and in 93.75% cases of pulmonary hemorrhage the neonate died.

Patients with CPAP failure had a greater death rate than neonates with CPAP success so, the relative risk was 2.51, and a similar pattern was seen for pulmonary hemorrhage (20.4% vs. 5.3%, relative risk: 2.51). in other words (16.1 % vs. 1.4 % , relative risk:14.04).[18] Surfactant therapy in babies with pulmonary bleeding, believed to be caused by a patent ductus arteriosus resulting in a sudden increase in pulmonary blood flow, has shown some encouraging outcomes in one study.[19] Recent studies have shown surfactant replacement treatment to be beneficial in and indicate that it may decrease infant mortality in low-resource settings. There should be sufficient personnel, professional capabilities, and infrastructure to administer surfactant and it should be used in conjunction with more cost-effective treatments such as prenatal steroids and early/delivery room CPAP in order to maximize benefits.[15-20] In addition, new techniques are always being researched and tried in order to make the surfactant administration process easier and the procedure itself less invasive.[21-23]

However, the adverse effects of surfactant, bradycardia, hypoxemia, and endotracheal tube occlusion, may occur during administration in the immediate aftermath. As a result, pulmonary compliance experiences significant alterations. After surfactant treatment, the incidence of lung hemorrhages may rise, although there has not been any evidence of a rise in the mortality rate associated with lung hemorrhages as all evidence currently points to treatment with surfactants lowering the mortality rate.[24, 25]

CONCLUSION

Administration of surfactant in term neonates, diagnosed with RDS, improved the survival outcomes of neonates and reduced complications of RDS. Thus, it can be implemented in neonatal facilities as a supportive treatment to reduce neonatal mortality.

Conflict of Interest: None

Authors Contribution

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

HZ & MTN: Data acquisition, critical review, approval of the final version to be published.

SH & AM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SZ & WA: Conception, data acquisition, 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.

REFERENCES

1. Hibbard JU, Wilkins I, Sun L, Gregory K, Haberman S, Hoffman M, et al. Respiratory morbidity in late preterm births. JAMA 2010; 304(4): 419. https://doi.org/10.1001/jama.2010.1015
2. Hermansen CL, Mahajan A. Newborn respiratory distress. Am Fam Physician 2015; 92(11): 994-1002.
3. Rao GC, Rao MSP. Etiological profile of respiratory distress in first day of life of a newborn baby. Int J Contemp Pediatr 2017; 4(1): 210-214. https://doi.org/10.18203/2349-3291.ijcp20164622
4. Niemarkt HJ, Hütten MC, Kramer BW. Surfactant for Respiratory Distress Syndrome: New Ideas on a Familiar Drug with Innovative Applications. Neonatology 2017; 111(4): 408-414. https://doi.org/10.1159/000464326
5. Khan EA, Hashmey I. Surfactant use in premature neonates <37 weeks gestation: Experience and outcome at a tertiary care hospital. J Pak Med Assoc 2015; 65(5): 486-490.
6. Soll R, Özek E. Multiple versus single doses of exogenous surfactant for the prevention or treatment of neonatal respiratory distress syndrome. Cochrane Database Syst Rev 2009(1): CD000141. https://doi.org/10.1002/14651858.CD000141.pub2
7. Pacifici GM. Effects of surfactants on preterm infant lungs. Med Express 2015;2. https://doi.org/10.5935/MedicalExpress.2015.02.03
8. Stevens TP, Blennow M, Myers EH, Soll R. Early surfactant administration with brief ventilation vs. selective surfactant and

continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. Cochrane Database Syst Rev 2007(4) :CD003063. https://doi.org/10.1002/14651858.CD003063.pub3
9. Gupta S, Donn SM. Novel Approaches to Surfactant Administration. Crit Care Res Pract 2012; 2012: 278483. https://doi.org/10.1155/2012/278483
10. Zapata HA, Fort P, Roberts KD, Kaluarachchi DC, Guthrie SO. Surfactant administration through laryngeal or supraglottic airways (SALSA): a viable method for low-income and middle-income countries. Front Pediatr 2022; 10: 853831. https://doi.org/10.3389/fped.2022.853831
11. Foglia EE, Jensen EA, Kirpalani H. Delivery room interventions to prevent bronchopulmonary dysplasia in extremely preterm infants. J Perinatol 2017; 37(11): 1171-1179. https://doi.org/10.1038/jp.2017.119
12. Tarawneh A, Kaczmarek J, Bottino MN, Sant'anna GM. Severe airway obstruction during surfactant administration using a standardized protocol: a prospective, observational study. J Perinatol 2012; 32(4): 270-275. https://doi.org/10.1038/jp.2011.101
13. Yen T-A, Wang C-C, Hsieh W-S, Chou H-C, Chen C-Y, Tsao P-N. Short-term outcome of pulmonary hemorrhage in very-low-birth-weight preterm infants. Pediatr Neonatol 2013; 54(5): 330-334. https://doi.org/10.1016/j.pedneo.2013.03.016
14. Ahmad KA, Bennett MM, Ahmad SF, Clark RH, Tolia VN. Morbidity and mortality with early pulmonary haemorrhage in preterm neonates. Arch Dis Child Fetal Neonatal Ed 2019; 104(1): F63. https://doi.org/10.1136/archdischild-2017-314611
15. Thukral A, Sankar M, Chandrasekaran A, Agarwal R, Paul V. Efficacy and safety of CPAP in low-and middle-income countries. J Perinatol 2016; 36(1): S21. https://doi.org/10.1038/jp.2016.30
16. Bozkaya A, Yurttutan S, Özkars MY, Doğaner A. Respiratory problems in preterm infants with pulmonary hemorrhage. J Matern Fetal Neonatal Med 2022 12; 35(25): 7505-7510. https://doi.org/10.1080/14767058.2021.1951207
17. Kültürsay N, Uygur Ö, Yalaz M. The use of surfactant in the neonatal period- the known aspects, those still under research and those which need to be investigated further. Turk Pediatri Ars 2014; 49(1): 1. https://doi.org/10.5152/tpa.2014.1267
18. Wang L, Li JH, Yu YH. Initial respiratory support modality and outcome in preterm infants with less than 32 weeks of gestation in China: A multicentre retrospective cohort study. Paediatr Perinat Epidemiol 2022; 36(3): 390-398. https://doi.org/10.1111/ppe.12801
19. Aziz A, Ohlsson A. Surfactant for pulmonary haemorrhage in neonates. Cochrane Database Syst Rev 2020; 2(2): CD005254. https://doi.org/10.1002/14651858.CD005254.pub3
20. Sankar M, Gupta N, Jain K, Agarwal R, Paul V. Efficacy and safety of surfactant replacement therapy for preterm neonates with respiratory distress syndrome in low-and middle-income countries: a systematic review. J Perinatol 2016; 36(1): S36-S48. https://doi.org/10.1038/jp.2016.32
21. Canals Candela FJ, Vizcaíno Díaz C, Ferrández Berenguer MJ, Serrano Robles MI, Vázquez Gomis C, Quiles Durá JL. [Surfactant replacement therapy with a minimally invasive technique: Experience in a tertiary hospital]. Ann Pediatr 2016; 84(2): 79-84. https://doi.org/10.1016/j.anpedi.2015.05.024
22. Nouraeyan N, Lambrinakos-Raymond A, Leone M, Sant'Anna G. Surfactant administration in neonates: A review of delivery methods. Can J Respir Ther 2014;50(3):91-95.
23. Aldana-Aguirre JC, Pinto M, Featherstone RM, Kumar M. Less invasive surfactant administration versus intubation for surfactant delivery in preterm infants with respiratory distress syndrome: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed 2017; 102(1): F17-F23 https://doi.org/10.1136/archdischild-2016-311936
24. Abdel-Latif ME, Osborn DA. Pharyngeal instillation of surfactant before the first breath for prevention of morbidity and mortality in preterm infants at risk of respiratory distress syndrome. Cochrane Database Syst Rev 2011(3): CD008311. https://doi.org/10.1002/14651858.CD008311.pub2
25. Speer CP. Neonatal respiratory distress syndrome: an inflammatory disease? Neonatology 2011; 99(4): 316-319. https://doi.org/10.1159/000320143