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Original Article

Effect of Lung Recruitment in the Efficacy of Intubation-Surfactant-Extubation Treatment of Respiratory Distress Syndrome in Preterm Neonates

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ABSTRACT

***Objectives*:** To compare the efficacy of lung recruitment versus conventional care in preterm neonates with respiratory distress syndrome in terms of reduction in requirement for mechanical ventilation.
***Study Design*:** Quasi-experimental study.
***Place and Duration of Study*:** Department of Pediatrics, Combined Military Hospital, Rawalpindi Pakistan, Mar 2022 to Mar 2023.
***Methodology*:** We conducted this study on 246 preterm neonates with respiratory distress syndrome. Neonates in the intervention arm received lung recruitment therapy with a pressure of 25 cmH2O for 15 seconds during surfactant administration. Both groups were subsequently placed on continuous positive pressure airway ventilation, failure of which was said to have occurred if the patient was unable to maintain SpO2 despite increasing FiO2 with worsening respiratory acidosis and apneic spells, which resulted in intubation and mechanical ventilation.
***Results*:** A total of 246 premature neonates with a mean gestational age at birth of 31.88±2.42 weeks were studied. Requirements for mechanical ventilation were seen in 29.3% of those who received lung recruitment versus 43.1% of those without (p=0.024). The total number of complicated cases was significantly lower with lung recruitment: 8.9% versus 17.9% in those without recruitment (p=0.040); however, the frequency of individual complications like pneumothorax (p=0.213), intraventricular hemorrhage (p=0.281), necrotizing enterocolitis (p=0.327) and mortality (p=0.254) were not significantly different across the groups.
***Conclusion*:** Using lung recruitment with administration of surfactant therapy for premature neonates is associated with reduced requirement for mechanical ventilation, duration of mechanical ventilation, and a reduction in total frequency of complications.

Keywords: Lung Recruitment, Mechanical Ventilation, Respiratory Distress Syndrome.

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INTRODUCTION

Neonatal respiratory distress syndrome (RDS) is the most common cause of morbidity and mortality in premature babies, affecting approximately 24,000 births per annum in the United States.[1] The disorder occurs due to a deficiency in the volume of surfactant, which fails to accumulate due to a shorter time of gestation, leading to alveolar collapse and failure of gas exchange after birth.[2] Management involves the application of continuous positive pressure airway ventilation with surfactant administration to prevent progression to the requirement for mechanical ventilation via the so-called INSURE method, where a neonate is Intubated, Surfactant is administered, and then the patient is Extubated.[3,4]

Various methods have been proposed to enhance surfactant penetration to distal alveoli, such as aerosolization via jet nebulization and ultrasonic techniques.[5,6] Lung recruitment is one such technique where the closed alveoli are opened by a short period of continuous distending pressure, allowing the surfactant to reach them: this is accomplished by a few methods such as patient positioning, maneuvers, and application of positive pressure to the lungs to force the alveoli open and creating a useful Functional Residual Capacity (FRC).[7-9] However, this process can result in injury to lung tissue through alveolar overdistention (volutrauma), critical airway pressures (barotrauma), and alveolar collapse and reopening (atelectotrauma), all of which can worsen the already compromised gas exchange and result in serious morbidity, and even mortality.[10]

We conducted this study to determine whether lung recruitment coupled with surfactant therapy in premature neonates with respiratory distress

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syndrome was associated with improved outcomes compared to surfactant therapy alone. If proven useful, this method could be adopted as a standard practice and help form the basis of a national consensus guideline for managing such patients, which currently does not exist.

METHODOLOGY

The quasi-experimental study was conducted from March 2022 to March 2023 from the Department of Paediatrics, Combined Military Hospital, Rawalpindi Pakistan, on 246 preterm neonates suffering from respiratory distress syndrome after obtaining consent for inclusion in the study from their parents/guardians. We selected the patients for our research via consecutive, non-probability sampling. The WHO sample size calculator was used to calculate the sample size, keeping an anticipated population proportion 1(P1) of 0.23 and an anticipated population proportion 2(P2) of 0.38, which were the proportions of patients requiring mechanical ventilation with surfactant therapy and lung recruitment versus conventional surfactant therapy alone, respectively, from Yang *et al*.[11]

Inclusion Criteria: Neonates born after the completion of 28 weeks of gestation but before the completion of the 37th week of gestation with respiratory distress syndrome, defined as a clinical syndrome of inadequate respiration manifested by respiratory rate >60 per minute with chest retractions and nasal flaring along with arterial blood gases showing a pH of less than 7.25, PaO2 <50 mmHg, and PaCO2 >45 mmHg, were included.

Exclusion Criteria: Patients with gross anatomical/ facial abnormalities, congenital heart disease, or those with birth asphyxia requiring intubation immediately on delivery in the labor room were excluded.

Patients were divided into two equal groups via block randomization and then intubated. Neonates in Group A received lung recruitment therapy via a T-piece resuscitator with a pressure of 25 cmH2O for 15 seconds, while those in Group B did not. Both groups received a 200 mg/kg dose of surfactant via the endotracheal tube (Figure).

Once the surfactant was administered, the neonates were extubated and placed on continuous positive-pressure airway ventilation (CPAP) at 6–8 cmH2O. If the patient required an inspired oxygen (FiO2) fraction of 0.4 or more to maintain SpO2 above 88% for longer than half an hour, or arterial blood gas testing revealed a pCO2 > 65 mmHg or the neonate had >4 apneic spells per hour, or more than two apneic spells requiring bag valve mask ventilation. CPAP was said to have failed, and the patient was placed on a mechanical ventilator.

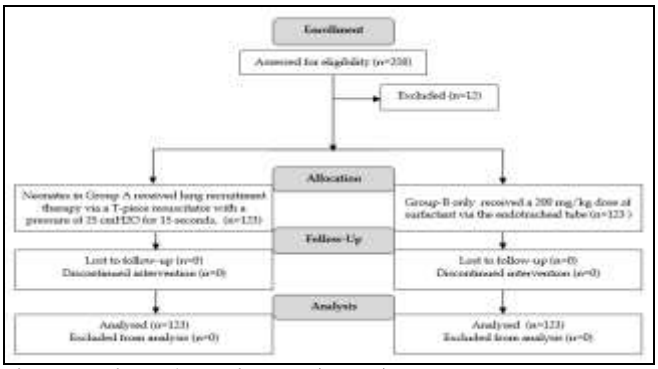

Figure: Patient Flow Diagram (n=246)

Mechanical ventilation was only stopped when the FiO2 requirement was less than 0.3, with a pCO2 ≤55 mmHg, a pH of ≥7.25, and SpO2 ≥88% for over eight hours. Following extubation, the neonates would be replaced on CPAP (6–8 cmH2O). If patients failed CPAP again, a further dose of surfactant at 100 mg/kg was given, with lung recruitment in the intervention arm. All patients were followed for seventy-two hours.

Data was analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows version 26, IBM Corp; Armonk, USA). Mean and standard deviation were calculated for quantitative variables, specifically gestational age at birth, birth weight, duration of requirement for mechanical ventilation, and maximum requirement for FiO2. Qualitative variables like gender, mode of delivery, predelivery corticosteroids given, the requirement for mechanical ventilation, and the occurrence of complications such as pneumothorax, intraventricular hemorrhage, necrotizing enterocolitis, and death were recorded in terms of frequency and percentage. Quantitative variables were compared across groups using the independent samples *t*-test. In contrast, the Chi-square test/Fischer exact test was used for qualitative variables, and a *p*-value of ≤0.05 was considered significant.

RESULTS

This study was conducted on 246 neonates with a mean gestational age at birth of 31.88±2.42 weeks with a male majority: 135(54.9%). The mean birth weight of the entire sample was 2001.66±387.54 g. The majority of patients were delivered vaginally: 147(59.8%).

Corticosteroids were administered to 192(78.0%) mothers pre-delivery. Table-I shows the patient characteristics at the time of enrollment in the study.

Table-I: Pre-Intervention Patient Characteristics (n=246)

Variables	Study Arm (n=123) Group-A	Control Arm (n=123) Group-B	*p*-value
Gender			
Male	61(49.6%)	74(60.2%)	0.096
Female	62(50.4%)	49(39.8%)	
Gestational Age (weeks)	31.70±2.44	32.06±2.40	0.248
Birth-weight (g)	1984.34±368.60	2018.98±406.36	0.485
Mode of Delivery			
Vaginal Delivery	69(56.1%)	78(63.4%)	0.242
Caesarean Section	54(43.9%)	45(36.6%)	
Pre-Delivery Corticosteroids	92(74.8%)	100(81.3%)	0.218

Table-II displays the outcomes of the study according to the study arm. The total requirement for mechanical ventilation was seen as 89(36.2%). The mean duration of the requirement for mechanical ventilation was 40.49±18.33 for hours for both arms. The mean FiO2 requirement for patients who required mechanical ventilation from the complete sample was 0.63±0.22%. A total of 33(13.4%) cases developed severe complications: 6(2.4%) developed a pneumothorax, 8(3.3%) developed an intraventricular hemorrhage, and 18(7.3%) developed necrotizing enterocolitis. 13(5.3%) patients died during the study period.

Table-II: Study Outcomes (n=246)

Variables	Study Arm (n=123) Group-A	Control Arm (n=123) Group-B	*p*-value
Requirement for Mechanical Ventilation	36(29.3%)	53(43.1%)	0.024
Duration of Ventilation Requirement (hours)	34.39±18.28	44.64±17.34	0.009
Maximum Requirement of FiO2	0.56±0.19	0.68±0.22	0.006
Complications			
Total Complicated Cases	11(8.9%)	22(17.9%)	0.040
Pneumothorax	1(0.8%)	5(4.1%)	0.213
Intraventricular Haemorrhage	2(1.6%)	6(4.8%)	0.281
Necrotizing Enterocolitis	7(5.7%)	11(8.9%)	0.327
Mortality	4(3.3%)	9(7.3%)	0.254

DISCUSSION

Neonatal RDS is a commonly occurring complication in newborns that is associated with a significant degree of morbidity and mortality not only due to the disease itself but also due to the treatment modalities, such as mechanical ventilation, used to manage it. Several techniques have been described to mitigate these effects, one of which is lung recruitment: our study demonstrated that this practice was associated with a decrease in the requirement for mechanical ventilation and a reduction in the total number of complications.

The mean gestational age at birth of our study sample was 31.88±2.42 weeks, which is in keeping with existing data on the subject, such as Mohapatra *et al*., and Kim *et al*., clearly demonstrate that the lower gestational age at birth; this higher the chances of developing neonatal RDS.[12,13] This occurs due to the deficient production of a surfactant or its inactivation due to fetal lung immaturity.[1]

The majority of patients in our study were male, 54.9%. Kim *et al*., reported that males were at an increased risk for developing RDS in their study (OR: 3.288; 95% CI, 1.446-7.479).[14] This has been attributed to the inhibitory effect of androgens on signal transduction, resulting in delayed fetal lung maturation and delayed fibroblast-pneumocyte factor production, resulting in delayed-type II alveolar cell maturation and surfactant production. In contrast, female sex hormones are proposed to do the opposite.[14]

The mean birth weight of our entire sample was 2001.66±387.54g Condò *et al*., noted in their study that low birth weight was associated with a higher risk of developing RDS in term neonates; however, this effect was less pronounced in preterm infants.[15] Whether this result is due to a confounding factor (preterm neonates are usually born with low birth weight) or not requires further study before concrete conclusions can be drawn.

Our study showed that the number of patients who required mechanical ventilation after receiving surfactant therapy with lung recruitment was 29.3%, significantly lower than in patients who received surfactant therapy without lung recruitment (p=0.024). Yang *et al*.,[11] reported that fewer patients who received surfactant therapy with lung recruitment required mechanical ventilation, i.e., 23% versus 38% in those that only received surfactant therapy (p=0.025), which was in agreement with our study, a finding which was also concurred with by Vento *et al*., who noted that 40% with surfactant plus recruitment required mechanical ventilation versus 54% with surfactant alone, (p=0.037).[16]

The present study demonstrated that patients who had received lung recruitment therapy had a shorter duration for the requirement for mechanical ventilation of 34.39±18.28 hours versus 44.64±17.34 hours for those who did not receive lung recruitment, (p=0.009), a result which was also agreed with by Yang *et al.,* (p=0.006).[11] Lista *et al.,* also noted that the total duration of the requirement for mechanical ventilation was significantly shorter with lung recruitment (p=0.008),[17] however, Jiravisitkul *et al.,* did not note this benefit, possibly because this study looked at lung recruitment without the use of surfactant.[18] Additionally, patients who received lung recruitment had a lower mean FiO2 requirement of 0.56±0.19 versus 0.68±0.22 in the control arm in our study (p=0.006), a result that was agreed with by both Yang *et al.,* and Vento *et al*.[11,16]

Our study showed that lung recruitment was associated with a decrease in total cases with complications, which were seen in 8.9% of cases. In comparison, the frequency of complicated cases was higher at 17.9% in the non-lung recruitment group (p=0.040). Our study did not demonstrate a significant difference in patients who received lung recruitment versus those without in terms of occurrence of pneumothorax (p=0.213), intraventricular hemorrhage (p=0.281), and necrotizing enterocolitis, (p=0.327), and mortality, (p=0.254), which was in keeping with the two other major studies on the subject, i.e., Yang *et al.,* and Vento *et al.,* both of whom noted that the frequency of each of their aforementioned complications, did not appear to be significantly different between the groups, however. In contrast, Yang *et al.,* noted no difference in mortality at the end of the follow-up period between the two groups; Vento *et al.,* pointed out that lung recruitment was associated with lower mortality, contrary to our study.[11,16] We attribute this difference to the duration of follow-up in each study: while the present study and Yang *et al.,* both had short follow-ups, Previous studies looked at patients for a more extended period, which may have affected results. Lung recruitment use is also associated with a reduction in the occurrence of total complications, which may improve the overall prognosis of the premature neonate.[17,18] However, this aspect of research requires further study and should be the focus of future research along with the long-term effects of lung recruitment on an individual's health.

CONCLUSION

Lung recruitment appears to be an effective modality in ensuring the delivery of surfactant across a greater surface area, which results in a reduction in the requirement for mechanical ventilation, a shorter duration of the requirement for mechanical ventilation, and a reduction in the degree of support required to maintain adequate tissue oxygenation and may be incorporated into the treatment of premature neonates with respiratory distress syndrome.

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Authors' Contribution

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

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

FI & SN: Conception, study design, drafting the manuscript, approval of the final version to be published.

MTN & BA: Data analysis, data interpretation, critical review, 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. Yadav S, Lee B, Kamity R. Neonatal Respiratory Distress Syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.
2. Chi M, Mei YB, Feng ZC. A review on neonatal acute respiratory distress syndrome. Zhongguo Dang Dai Er Ke Za Zhi 2018; 20(9): 724-728. https://doi.org/10.7499/j.issn.1008-8830.2018.09.006
3. Ekhaguere OA, Okonkwo IR, Batra M, Hedstrom AB. Respiratory distress syndrome management in resource limited settings-Current evidence and opportunities in 2022. Front Pediatr 2022; 10(1): 961509. https://doi.org/10.3389/fped.2022.961509
4. Jena SR, Bains HS, Pandita A, Verma A, Gupta V, Kallem VR, et al, On Behalf Of Sure Group. Surfactant therapy in premature babies: SurE or InSurE. Pediatr Pulmonol 2019; 54(11): 1747-1752. https://doi.org/10.1002/ppul.24479
5. Goss KC, Gale C, Malone R, Longford N, Ratcliffe K, Modi N. Effect of surfactant dose on outcomes in preterm infants with respiratory distress syndrome: the OPTI-SURF study protocol. BMJ Open 2020; 10(12): e038959. https://doi.org/10.1136/bmjopen-2020-038959
6. Kamga-Gninzeko FJ, Valentine MS, Tho CK, Chindal SR, Boc S, Dhapare S, et al. Excipient Enhanced Growth Aerosol Surfactant Replacement Therapy in an In Vivo Rat Lung Injury Model. J Aerosol Med Pulm Drug Deliv 2020; 33(6): 314-322. https://doi.org/10.1089/jamp.2020.1593
7. Herman L, De Smedt SC, Raemdonck K. Pulmonary surfactant as a versatile biomaterial to fight COVID-19. J Control Release 2022; 342(1): 170-188. https://doi.org/10.1016/j.jconrel.2021.11.023
8. Konduri GG, Lakshminrusimha S. Surf early to higher tides: surfactant therapy to optimize tidal volume, lung recruitment, and iNO response. J Perinatol 2021; 41(1): 1-3. https://doi.org/10.1038/s41372-020-0764-4

9. Ekhaguere OA, Okonkwo IR, Batra M, Hedstrom AB. Respiratory distress syndrome management in resource limited settings-Current evidence and opportunities in 2022. Front Pediatr 2022; 10(1): 961509. https://doi.org/10.3389/fped.2022.961509
10. Peel JK, Funk DJ, Slinger P, Srinathan S, Kidane B. Positive end-expiratory pressure and recruitment maneuvers during one-lung ventilation: A systematic review and meta-analysis. J Thorac Cardiovasc Surg 2020; 160(4): 1112-1122.e3. https://doi.org/10.1016/j.jtcvs.2020.02.077
11. Yang Y, Yan W, Ruan M, Zhang L, Su J, Deng H, et al. Lung recruitment improves the efficacy of intubation-surfactant-extubation treatment for respiratory distress syndrome in preterm neonates, a randomized controlled trial. BMC Pediatr 2022; 22(1): 14. https://doi.org/10.1186/s12887-021-03096-y
12. Mohapatra V, Saraogi S, Misra S. Demographic Profile, Etiology, and Perinatal Outcome Associated With Preterm Birth in a Tertiary Hospital of Eastern India: A Retrospective Study. Cureus 2022; 14(6): e26066. https://doi.org/10.7759/cureus.26066
13. Kim JK, Hwang JH, Lee MH, Chang YS, Park WS. Mortality rate-dependent variations in antenatal corticosteroid-associated outcomes in very low birth weight infants with 23-34 weeks of gestation: A nationwide cohort study. PLoS One 2020; 15(10): e0240168. https://doi.org/10.1371/journal.pone.0240168
14. Kim JH, Lee SM, Lee YH. Risk factors for respiratory distress syndrome in full-term neonates. Yeungnam Univ J Med 2018; 35(2): 187-191. https://doi.org/10.12701/yujm.2018.35.2.187
15. Condò V, Cipriani S, Colnaghi M, Bellù R, Zanini R, Bulfoni C, et al. Neonatal respiratory distress syndrome: are risk factors the same in preterm and term infants? J Matern Fetal Neonatal Med 2017; 30(11): 1267-1272. https://doi.org/10.1080/14767058.2016.1210597
16. Vento G, Ventura ML, Pastorino R, van Kaam AH, Carnielli V, Cools F, et al. Lung recruitment before surfactant administration in extremely preterm neonates with respiratory distress syndrome (IN-REC-SUR-E): a randomised, unblinded, controlled trial. Lancet Respir Med 2021; 9(2): 159-166. https://doi.org/10.1016/S2213-2600(20)30179-X
17. Lista G, Fontana P, Castoldi F, Cavigioli F, Dani C. Does sustained lung inflation at birth improve outcome of preterm infants at risk for respiratory distress syndrome? Neonatology 2011; 99(1): 45-50. https://doi.org/10.1159/000298312
18. Jiravisitkul P, Rattanasiri S, Nuntnarumit P. Randomised controlled trial of sustained lung inflation for resuscitation of preterm infants in the delivery room. Resuscitation 2017; 111(1): 68-73. https://doi.org/10.1016/j.resuscitation.2016.12.003