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Original Research Article

A Non-Randomized Controlled Trial to Examine the Effectiveness of Surfactant in Preterm Infants 32-36 Weeks Gestation with RDS Grade I and II

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Abstract

Aim: The aim of the present study was to examine the effectiveness of surfactant in preterm infants 32-36 weeks gestation with RDS grade I and II.

Methods: A non-randomized controlled trial conducted in the Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India from August 2018 to July 2019. RDS was identified based on clinical characteristics and chest X-ray results. During the research period, 161 preterm neonates with a gestational age more than 32 weeks were admitted to the NICU. On the basis of clinical and radiological characteristics, Grade I, II, 66 children born prematurely were diagnosed with respiratory distress syndrome RDS.

Results: The surfactant group included 39 (59.1%) premature infants, 22(56.4%) males, 17(43.7%) females and the non-surfactant group included 27(40.1%) premature infants, 15(55.6%) males, 12 (44.4%) females. Mean gestational age (34.46±1.12 vs. 34.48±1.09 weeks) and mean birth weight (1924.79±322.78 vs. 1925.93±322.36 g) were similar between the Surfactant group and non-surfactant group. The difference between the Surfactant group and non-surfactant group in gender, gestational age and birth weight was not statistically significant. The difference was not statistically significant. Occurred in 6 preterm infants had, 4 preterm infants in the surfactant group (10.3%) and 2 preterm infants in the non-surfactant group, the difference was not statistically significant. Hospitalization time was ≤ one week for 27 infants in the surfactant group (69.2%) and for 14 infants in the non-surfactant group (51.9%), while the hospitalization time was > one week for 12 infants in the surfactant group (30.8%) and for 13 infants in the non-surfactant group (48.1%), the difference was not statistically significant.

Conclusion: This study indicated that newborns with RDS grades I and II and gestational ages between 32 and 36 weeks who were administered surfactant had results comparable to those of infants who were not given surfactant.

Keywords: Pulmonary surfactant factor, respiratory distress syndrome, premature

Introduction

Surfactant administration for the treatment of respiratory distress syndrome (RDS) is the mainstay intervention to reduce mortality and major morbidity in preterm neonates. [1] Since the first clinical trial performed in 1980, significant progress has been made with respect to its use. [2] Systematic reviews indicate that early surfactant administration and the use of lesser invasive modalities such as less invasive surfactant administration (LISA) reduce mortality and the risk of bronchopulmonary dysplasia (BPD). However, there is a paucity of evidence to define the optimal thresholds at which exogenous surfactant therapy would be most effective. [1,3-5]

Our current understanding is that the pathophysiology of RDS is multifactorial, of which surfactant deficiency remains the most important aspect. [6] In the absence of a clinically feasible test to accurately and timely quantify surfactant levels in the preterm lung, several other markers have been used to classify the severity of RDS. Of these, the fraction of inspired oxygen (FiO2) requirement is most used. To date, there are no randomized controlled trials (RCT) evaluating different FiO2 thresholds together with defined modalities of surfactant administration in preterm neonates with RDS who are stabilized on CPAP. [7,8]

This lacuna is evident in the differing recommendations by various international RDS treatment guidelines, focusing predominantly on oxygen requirement to maintain acceptable peripheral saturations (SpO2). [3,9] However, apart from FiO2 there may be other parameters available to predict significant RDS and guide targeted surfactant administration, ideally during an optimal time frame. Other parameters for predicting the severity of RDS that have been studied include arterial alveolar oxygen tension ratio (a/AO2), lamellar body counts in lung- or gastric aspirates, lung ultrasound and clinical scoring systems of respiratory distress. [8,10-12]

The aim of the present study was to examine the effectiveness of surfactant in preterm infants 32-36 weeks gestation with RDS grade I and II.

Materials and Methods

A non-randomized controlled trial (NRS) conducted in the Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India from August 2018 to July 2019. RDS was identified based on clinical characteristics and chest X-ray results. During the research period, 161 preterm neonates with a gestational age more than 32 weeks were admitted to the NICU. On the basis of clinical and radiological characteristics, Grade I, II, 66 children born prematurely were diagnosed with respiratory distress syndrome RDS.

All preterm infants (born in the delivery room or operating room with spontaneous breathing but respiratory distress at birth) were administered NCPAP to stabilize their breathing condition, beginning with a resuscitator at positive end expiratory pressure levels of 5-10 cmH2O and continuing during transfer to the NICU. In addition to using a nasal prong and inserting an orogastric tube to prevent belly distension, cardiopulmonary monitoring was also undertaken. The amount of continuous positive airway pressure (CPAP) varied between 5 and 8 cmH2O, and FiO2 was regulated to maintain 90-95% oxygen saturation. Surfactant is administered if clinical improvement does not occur within 6 hours or if babies require FiO2 > 40% to maintain arterial oxygen saturation (endotracheal tube). 39(59.1%) babies were treated with surfactant (single dose of Survanta @ 100 mg/kg = 4 ml/Kg) (natural bovine lung lavage) and Continuous Positive Airway Pressure (CPAP). Respiratory distress syndrome grade III, IV, any congenital deformity, inherited metabolic abnormalities, intrauterine infection, Rh/Rh incompatibility, pneumonia, pulmonary hypertension, meconium aspiration syndrome, asphyxia, and early onset sepsis are the exclusion criteria. Collecting data; Data were collected regarding gender, gestational age, birth weight, and complications (intraventricular hemorrhage, pulmonary hemorrhage, pneumothorax, necrotizing enterocolitis, retinopathy of prematurity, and late onset sepsis), duration of treatment (less or more than a week), and the end point was death or improvement and discharge of the premature infant. Analyses based on descriptive statistics, including mean and standard deviation (SD) expressions for quantitative variables, and ratio and percentage expressions for qualitative variables. Quantitative and qualitative factors were analyzed using the Student t test and chi-square test, respectively. In this study, IBM SPSS Statistics version 20.0 was utilised for data analysis. The statistical significance threshold was determined to be P0.05. Ethical permission; the newborn parents gave their written consent to participate in the investigation. Additionally, no private information was disclosed.

Results

Table 1: Comparison of the demographic characteristics of newborns between the Surfactant group and non-surfactant group

	Surfactant (39)		Non-Surfactant (27)		p-value
	No/Mean	%/SD	No/Mean	%/SD	
Female	17	43.6	12	44.4	0.945
Male	22	56.4	15	55.6	
Gestational age (weeks)	34.46	1.12	34.48	1.09	0.943
Birth weight (g)	1924.79	322.78	1925.93	322.36	0.959

The surfactant group included 39 (59.1%) premature infants, 22(56.4%) males, 17(43.7%) females and the non-surfactant group included 27(40.1%) premature infants, 15(55.6%) males, 12 (44.4%) females. Mean gestational age (34.46±1.12 vs. 34.48±1.09 weeks) and mean birth weight (1924.79±322.78 vs. 1925.93±322.36 g) were similar between the Surfactant group and non-surfactant group. The difference between the Surfactant group and non-surfactant group in gender, gestational age and birth weight was not statistically significant.

Table 2: Severity of RDS in the Surfactant group and non-surfactant group

	Surfactant (39)		Non-Surfactant (27)		p-value
	No	%	No	%	
RDS grade I	11	28.2	8	29.6	0.900
RDS grade II	28	71.8	19	70.4	

In surfactant group 11(28.2%) preterm infants had RDS grade I and 28 (71.8%) preterm infants had RDS grade II. In non-surfactant group 8(29.6%) preterm infants with RDS Grade I and 19(70.4%) premature infants with RDS grade II, the difference was not statistically significant.

Table 3: Comparison of complications between the Surfactant group and non-surfactant group

	Surfactant (39)		Non-Surfactant (27)		p-value
	No/Mean	%/SD	No/Mean	%/SD	
IVH	8	20.5	2	7.4	0.144
Pulmonary Hemorrhage	3	7.7	1	3.7	0.504
Pneumothorax	4	10.3	2	7.4	0.692
NEC	3	7.7	7	25.9	0.042
ROP	0	0	1	3.7	0.226
LOS	9	23.1	6	22.2	0.935

Occurred in 6 preterm infants had, 4 preterm infants in the surfactant group (10.3%) and 2 preterm infants in the non-surfactant group, the difference was not statistically significant. Necrotizing enterocolitis (NEC): Occurred in 10 preterm infants, whereas in the surfactant group 3 infants (7.7%), while in the non-surfactant group 7 infants (25.9%), the difference was statistically significant. One premature infant in the non-surfactant group (3.7%) had retinopathy of prematurity. Late Onset Sepsis (LOS): Occurred in 15 preterm infants, 9 preterm infants in the surfactant group (23.1%) and 6 preterm infants in the non-surfactant group (22.2%), the difference was not statistically significant.

Table 4: Comparison of outcomes between the Surfactant group and non-surfactant group

		Surfactant (39)		Control (27)		p-value
		No./ Mean	%/SD	No./ Mean	%/SD	
Hospitalization time	≤ one week	27	69.2	14	51.9	0.152
	> one week	12	30.8	13	48.1	
Death		1	2.6	1	3.7	0.791
Survival		38	97.4	26	96.3	

Hospitalization time was ≤ one week for 27 infants in the surfactant group (69.2%) and for 14 infants in the non-surfactant group (51.9%), while the hospitalization time was > one week for 12 infants in the surfactant group (30.8%) and for 13 infants in the non-surfactant group (48.1%), the difference was not statistically significant. The survival rate in the surfactant group was 97.4% (38 infants), and in the non-surfactant group was 96.3% (26 infants), the difference was not statistically significant. One premature infant in the surfactant group died after 3 days of admission, where he had IVH grade 3, pulmonary hemorrhage and pneumothorax. One premature infant in the non-surfactant group died after 13 days of admission, where he had pulmonary hemorrhage and late onset sepsis leading to septic shock and disseminated intravascular coagulopathy (DIC).

Discussion

Preterm infants are born before 37 weeks' gestation. Extreme preterm birth occurs before 28 weeks, extremely preterm birth between 28-32 weeks, and moderate to late preterm delivery between 32-37 weeks. [13] Preterm delivery problems kill 1 million children annually. Many survivors have learning impairments, vision and hearing issues for life. [14] Premature babies are more likely to suffer RDS, cerebral palsy, developmental delays, hearing and visual difficulties. Early birth increases these risks. [15] RDS, originally called hyaline membrane disorder, is frequent in premature babies. RDS is caused by immature pulmonary surfactant. RDS causes morbidity and death in premature babies. [16]

The surfactant group included 39 (59.1%) premature infants, 22(56.4%) males, 17(43.7%) females and the non-surfactant group included 27(40.1%) premature infants, 15(55.6%) males, 12 (44.4%) females. Mean gestational age (34.46±1.12 vs. 34.48±1.09 weeks) and mean birth weight (1924.79±322.78 vs. 1925.93±322.36 g) were similar between the Surfactant group and non-surfactant group. The difference between the Surfactant group and Non-Surfactant group in gender, gestational age and birth weight was not statistically significant. In surfactant group

11(28.2%) preterm infants had RDS grade I and 28 (71.8%) preterm infants had RDS grade II. In non-surfactant group 8(29.6%) preterm infants with RDS Grade I and 19(70.4%) premature infants with RDS grade II, the difference was not statistically significant. Occurred in 6 preterm infants had, 4 preterm infants in the surfactant group (10.3%) and 2 preterm infants in the non-surfactant group, the difference was not statistically significant. Necrotizing enterocolitis (NEC): Occurred in 10 preterm infants, whereas in the surfactant group 3 infants (7.7%), while in the non-surfactant group 7 infants (25.9%), the difference was statistically significant. One premature infant in the non-surfactant group (3.7%) had retinopathy of prematurity. Late Onset Sepsis (LOS): Occurred in 15 preterm infants, 9 preterm infants in the surfactant group (23.1%) and 6 preterm infants in the non-surfactant group (22.2%), the difference was not statistically significant. Hospitalization time was ≤ one week for 27 infants in the surfactant group (69.2%) and for 14 infants in the non-surfactant group (51.9%), while the hospitalization time was > one week for 12 infants in the surfactant group (30.8%) and for 13 infants in the non-surfactant group (48.1%), the difference was not statistically significant. The survival rate in the surfactant group was 97.4% (38 infants), and in the non-surfactant group was 96.3% (26 infants), the difference was not statistically significant. Jackson et al. research, which comprised 54964 preterm children with gestational age 30-36 weeks of gestational age and birth weight > 2 kg with RDS. There was no significant correlation between surfactant therapy and reduced mortality or morbidity in preterm babies with GA more than 30 weeks who had RDS and who were treated with surfactant (46%). [17] Wang et al. discovered a trend toward decreased hospitalization time with increasing gestational age, but a trend toward an increased rate of repeated surfactant administration with increasing gestational age; additionally, surfactant replacement therapy for RDS was more effective in premature infants 35 weeks' gestational age than in near-term and term infants. [18]

One premature infant in the surfactant group died after 3 days of admission, where he had IVH grade 3, pulmonary hemorrhage and pneumothorax. One premature infant in the non-surfactant group died after 13 days of admission, where he had pulmonary hemorrhage and late onset sepsis leading to septic shock and disseminated intravascular coagulopathy (DIC). Helve et al. observed that RDS due to surfactant deficit was most prevalent in babies with a gestational age of 35 weeks and that RDS due to the delayed evacuation of lung fluid was more prevalent in full and near-term infants than in preterm infants. [19] In a retrospective study by Coshal, et al. (included 8594 neonates of 29 weeks' GA) was compared the outcomes of using surfactant (one or more doses) with the non-use of surfactant, with surfactant therapy administration according to recommendations made by the Canadian Pediatric Society to ensure safety and accuracy (administration of surfactant to intubated patients with RDS, prophylactic administration after stabilisation in intubated preterm neonates at significant risk of RDS). They discovered that neonates who received one or multiple doses of surfactant had higher odds of mortality and major morbidities (specifically severe neurological injury, BPD, and stage 3 or higher ROP) compared to those who did not receive surfactant. [20]

Conclusion

This study indicated that newborns with RDS grades I and II and gestational ages between 32 and 36 weeks who were administered surfactant had results comparable to those of infants who were not given surfactant.

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