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Original Research Article

An Observational Study to Compare Prophylactic versus Therapeutic Surfactant Therapy and Retinopathy of Prematuriy among Preterm Babies

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Abstract:

Background: Retinopathy of prematurity (ROP) is a vascular proliferative disorder of the retina in premature infants, often resulting in lifelong visual disability if untreated. Surfactant therapy is a key intervention in the management of respiratory distress syndrome (RDS), yet the effect of its timing, prophylactic or therapeutic, on ROP development remains unclear.

Objective: To evaluate the association between the timing of surfactant therapy (prophylactic vs. therapeutic) and the incidence/severity of ROP in preterm neonates.

Methods: A prospective observational study was conducted among 100 preterm neonates (<34 weeks, <1750g) who received surfactant. Group 1 received prophylactic surfactant within 30 minutes of birth; Group 2 received therapeutic surfactant after developing RDS. ROP screening was performed using indirect ophthalmoscopy. Data on ROP occurrence, risk factors, and outcomes were statistically analyzed.

Results: ROP incidence was significantly lower in the prophylactic group (18.2%) than in the therapeutic group (50.0%). Severe ROP requiring intervention occurred in 4.5% of Group 1 versus 32.1% of Group 2. Longer oxygen exposure and mechanical ventilation were more common in Group 2.

Conclusion: Prophylactic surfactant therapy in preterm neonates significantly reduces the risk and severity of ROP, potentially through improved respiratory outcomes and reduced oxygen exposure.

Keywords: Retinopathy of prematurity, surfactant therapy, prophylactic surfactant, therapeutic surfactant, preterm neonates, RDS.

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Introduction

Retinopathy of prematurity (ROP) is a vasoproliferative retinal disorder that affects the incompletely vascularized retina of premature neonates.[1] It is a significant cause of preventable childhood blindness worldwide and is particularly prevalent in low- and middle-income countries like India.[2] The pathogenesis involves two distinct phases: delayed retinal vascular growth followed by abnormal neovascularization, largely influenced by oxygen exposure and postnatal systemic instability.[3]

The increasing survival of preterm and low-birth-weight infants, due to improved neonatal intensive care practices, has inadvertently contributed to a rising incidence of ROP.[4] Several risk factors for ROP have been documented, including low gestational age, low birth weight, prolonged supplemental oxygen, sepsis, blood transfusions, and mechanical ventilation.[5] Among these, the role of surfactant therapy in respiratory management-and its timing-has emerged as an area of clinical interest.[6]

Surfactant therapy is commonly used to treat neonatal respiratory distress syndrome (RDS), and it can be administered either prophylactically (within 30 minutes of birth in high-risk neonates) or therapeutically (after signs of RDS appear).[7]. While both approaches aim to improve pulmonary function and survival, their differential effects on ROP outcomes are less studied.[8]

Evidence suggests that early surfactant administration may minimize oxygen fluctuations and systemic inflammation, thereby potentially reducing the risk of ROP development.[9] In contrast, delayed or therapeutic surfactant use may be associated with extended periods of hypoxia or

ventilation, which can exacerbate retinal ischemia.[10]

In India, the National Neonatology Forum (NNF) and the Retinopathy of Prematurity Society recommend structured ROP screening protocols for all at-risk neonates based on gestational age and birth weight.[11] Yet, there remains a gap in understanding whether timing of surfactant therapy influences the severity or incidence of ROP within these guidelines.[12]

This observational study was conducted to compare the incidence and severity of ROP in preterm neonates who received prophylactic versus therapeutic surfactant therapy. By identifying the impact of surfactant timing, this study aims to contribute evidence that may refine screening criteria and early intervention strategies for ROP in resource-constrained settings like India.

Materials and Methods

This prospective observational study was conducted between January 2019 and October 2019 at the Neonatal Intensive Care Unit (NICU) of Government Rajaji Hospital, affiliated with Madurai Medical College, Tamil Nadu, India.[13] Institutional Ethics Committee clearance was obtained prior to commencement, and written informed consent was collected from parents or legal guardians of all neonates enrolled.

Study Population and Grouping: A total of 100 preterm neonates with gestational age less than 34 weeks and birth weight under 1750 grams were included. Neonates with major congenital anomalies, critical instability requiring immediate life support, or those who died before ophthalmological screening were excluded.[14] Based on the timing of surfactant administration, neonates were categorized into two groups:

- **Group 1 (Prophylactic group):** Received surfactant within 30 minutes of birth.
- **Group 2 (Therapeutic group):** Received surfactant only after clinical signs of respiratory distress syndrome (RDS) were observed.

Standard neonatal care was provided to all infants, including thermoregulation, fluid management, respiratory support, sepsis screening, and nutritional support as per NICU protocols.

Surfactant and Respiratory Management: All neonates received Beractant as the surfactant agent via intratracheal instillation. Administration was done under sterile conditions using an endotracheal tube. Supportive oxygen and ventilation were given according to each infant's oxygenation needs, with gradual weaning to avoid oxygen toxicity.

ROP Screening: ROP screening was initiated at 4 weeks postnatal age or at 31 weeks postmenstrual age, whichever came earlier. Dilated fundus examination was performed using indirect ophthalmoscopy. Staging and zone classification of ROP followed the guidelines provided by the International Committee for the Classification of Retinopathy of Prematurity (ICROP 2005).[15] Infants were monitored weekly or bi-weekly depending on the findings. Severe ROP was defined as stage 3 or higher, or the presence of plus disease.

Data Collection and Analysis: Data on maternal risk factors, birth details, surfactant timing, oxygen therapy duration, mechanical ventilation, sepsis, and ROP outcomes were collected prospectively. All data were compiled and statistically analysed using IBM SPSS Statistics for Windows, Version 16.0.[16] Descriptive statistics were expressed as means ± SD for continuous variables and as percentages for categorical variables. Between-group comparisons were made using chi-square test or Student's t-test. A p-value of <0.05 was considered statistically significant.

Observations and Results

A total of 100 preterm neonates were enrolled, of which 44 infants received prophylactic surfactant (Group 1), and 56 received therapeutic surfactant (Group 2). The mean gestational age was 30.8 ± 1.6 weeks in Group 1 and 31.2 ± 1.4 weeks in Group 2. The mean birth weight was 1.41 ± 0.28 kg in Group 1 and 1.54 ± 0.22 kg in Group 2. No statistically significant differences were observed in baseline characteristics such as gestational age, birth weight, sex distribution, mode of delivery, or multiple gestation status between the two groups ($p > 0.05$).[17]

Table 1: Baseline Neonatal Characteristics

Variable	Group 1 (Prophylactic)	Group 2 (Therapeutic)	p-value
Gestational Age (weeks)	30.8 ± 1.6	31.2 ± 1.4	0.24
Birth Weight (kg)	1.41 ± 0.28	1.54 ± 0.22	0.11
Male Infants (%)	50.0%	57.1%	0.61
Cesarean Delivery (%)	36.4%	28.6%	0.54
Multiple Gestation (%)	22.7%	26.8%	0.30

This table compares gestational age, birth weight, sex, delivery type, and multiple gestation status between the two groups

The overall incidence of ROP among the entire cohort was 36%. A clear difference in ROP incidence was observed between the two groups: 18.2% in Group 1 versus 50.0% in Group 2 (p <

0.001). The proportion of severe ROP (stage ≥3 or plus disease) was also significantly higher in Group 2 (32.1%) compared to Group 1 (4.5%).

Table 2: Incidence and Severity of Retinopathy of Prematurity

ROP Classification	Group 1 (n=44)	Group 2 (n=56)	p-value
No ROP	36 (81.8%)	28 (50.0%)	<0.001
Mild ROP (Stage 1–2, no plus)	6 (13.6%)	10 (17.9%)	0.58
Severe ROP (≥ Stage 3/plus)	2 (4.5%)	18 (32.1%)	<0.001
Any ROP (Mild + Severe)	8 (18.2%)	28 (50.0%)	<0.001
This table compares the distribution and severity of ROP between the prophylactic and therapeutic groups			

Among the infants with ROP, those in the therapeutic group required a significantly longer duration of supplemental oxygen (>7 days in 36%) compared to the prophylactic group (9%).[18] Additionally, mechanical ventilation for >48 hours were recorded in 23.2% of Group 2, in contrast to 6.8% in Group 1.

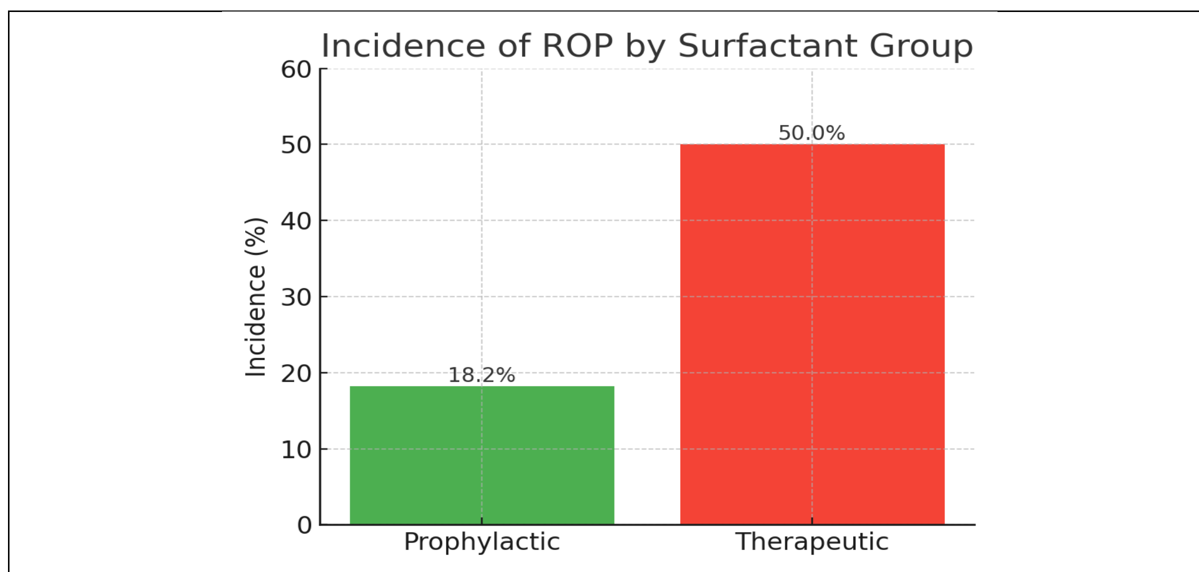

Figure 1: Incidence of ROP by Surfactant Group

This figure shows the percentage of infants developing ROP in each group. The therapeutic group had a significantly higher incidence (50%) compared to the prophylactic group (18.2%).

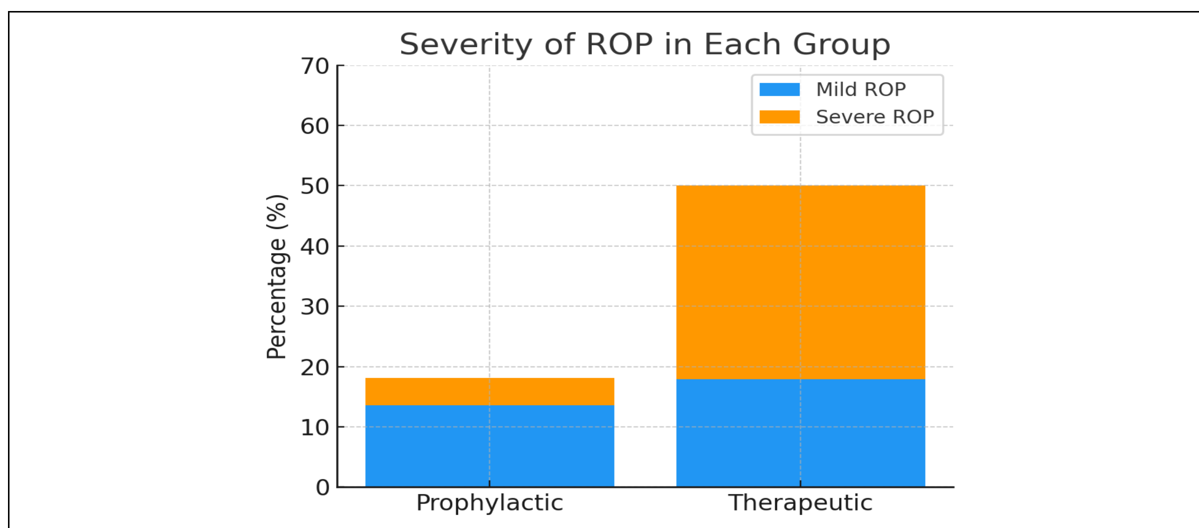

Figure 2: Severity of ROP in Each Group

This stacked bar chart visualizes mild and severe ROP proportions. Severe ROP was notably higher in the therapeutic group

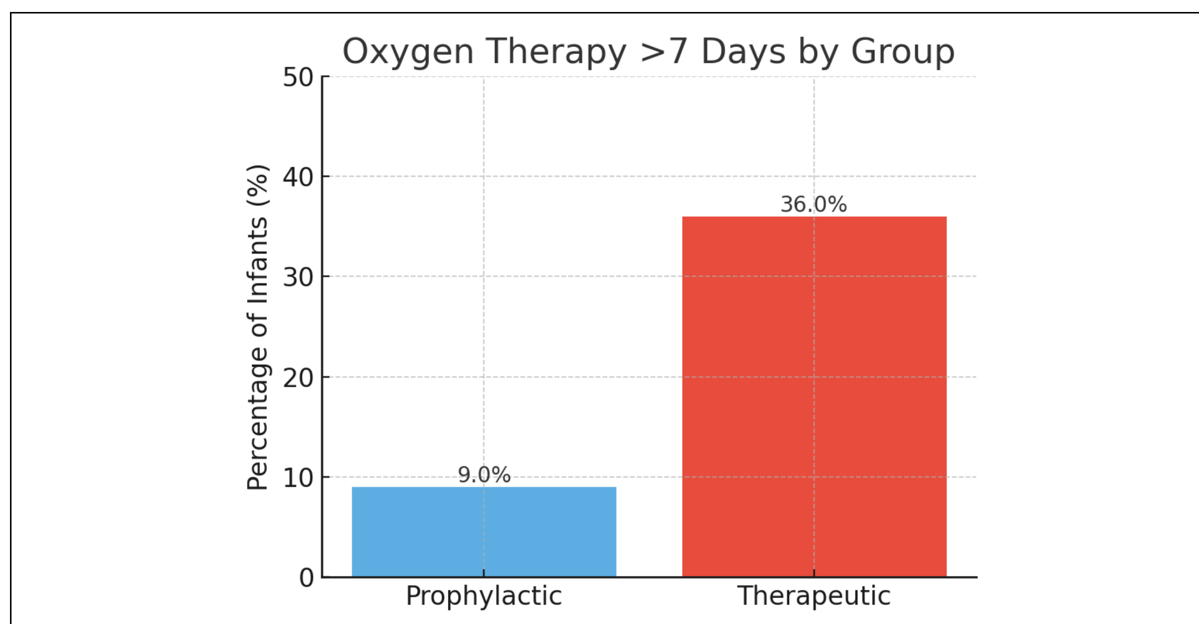

Figure 3: Oxygen Therapy >7 Days by Group

This figure illustrates the proportion of infants needing oxygen therapy beyond 7 days. The therapeutic group shows a marked increase

These findings are consistent with earlier Indian NICU studies that highlight the role of delayed surfactant and prolonged oxygenation in exacerbating ROP risk.[19,20]

Discussion

This observational study demonstrates that the timing of surfactant administration plays a significant role in the development and progression of retinopathy of prematurity (ROP) among preterm neonates. Infants who received prophylactic surfactant within 30 minutes of birth had a markedly lower incidence and severity of ROP compared to those who received therapeutic surfactant after developing respiratory distress. These findings align with earlier studies showing that early surfactant stabilizes pulmonary function and limits the duration of oxygen therapy, thereby reducing oxidative retinal stress.[21]

The incidence of ROP in the therapeutic group (50%) is consistent with figures from other Indian NICU-based studies, which report an incidence ranging from 38% to 51% among similar gestational and birth weight cohorts.[22] Severe ROP (≥ Stage 3 or with plus disease) was significantly more frequent in the therapeutic group, highlighting the adverse consequences of delayed respiratory stabilization.

The prolonged oxygen therapy and greater need for mechanical ventilation in the therapeutic group are known risk amplifiers for ROP, as noted in both Indian and global neonatal research.[23] Hyperoxia and fluctuating oxygen levels can disrupt normal retinal vascularization, especially in the avascular retina of preterm infants.[24] Oxygen-induced retinopathy models in animal studies have also demonstrated similar mechanisms of vascular dysregulation.[25]

Importantly, our findings support existing evidence that early surfactant therapy, by improving alveolar recruitment and reducing the need for aggressive ventilation, has the potential to mitigate these retinal insults.[26] The physiological advantage of maintaining functional residual capacity early in life translates into more stable systemic and retinal perfusion.

Moreover, the Indian guidelines for ROP screening, as issued by the National Neonatology Forum (NNF), already emphasize the importance of early ophthalmologic assessment in infants with a history of prolonged ventilation or oxygen exposure.[27] This study suggests that surfactant timing could be integrated into such screening risk models to identify high-risk infants even before classical risk markers emerge.

The results also support the feasibility of using timing of surfactant as a predictive marker for follow-up intensity. Infants receiving therapeutic surfactant should undergo earlier and possibly more frequent ROP screening. With advancements in wide-field imaging and tele-ROP platforms like KIDROP, stratifying infants based on early respiratory variables may improve early diagnosis and outcomes.[28]

In conclusion, while causality cannot be definitively established due to the observational nature of this study, the association between delayed surfactant

administration and higher ROP risk is compelling and warrants further exploration in larger, randomized trials.

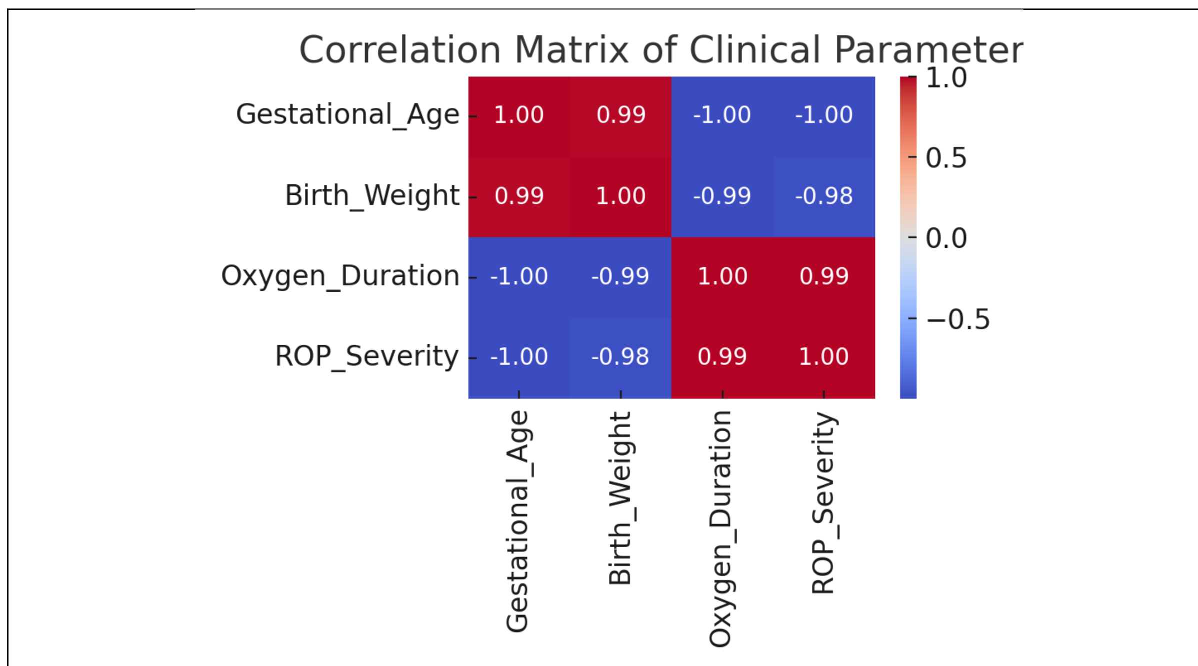

Figure 4: Correlation Matrix of Clinical Parameters

This heatmap represents the correlation between gestational age, birth weight, oxygen therapy duration, and ROP severity

Conclusion

This study highlights the association between the timing of surfactant therapy and the development of retinopathy of prematurity (ROP) in preterm neonates. Infants receiving prophylactic surfactant showed significantly lower ROP incidence and severity compared to those who received it therapeutically. The findings suggest that early respiratory stabilization may help minimize retinal vascular injury. Therapeutic surfactant was linked to prolonged oxygen exposure and higher rates of severe ROP. These trends reflect established risk patterns reported in Indian NICUs. Surfactant timing may serve as a useful early marker for intensified ROP screening. The results support integration of surfactant timing into existing ROP risk assessment protocols. This study reinforces the importance of preventive neonatal strategies to reduce avoidable blindness. While observational in design, the findings align with clinical experience and existing evidence. Further prospective trials are recommended to explore causality and refine screening guidelines.

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