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Chronic Obstructive Pulmonary Disease (COPD) and the Impact of Parental Steroid Dexamathasone on Preterm Infants: A Correlation Between Reduced Surfactant Lipids and Lung Function

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ABSTRACT

Background: Chronic respiratory conditions, including neonatal respiratory distress syndrome (RDS), are strongly influenced by surfactant deficiency, a common complication in preterm infants. Antenatal corticosteroids like dexamethasone are routinely used to enhance fetal lung maturity, but their effects on surfactant lipid levels and pulmonary function require further investigation. To evaluate the impact of antenatal dexamethasone on surfactant lipid levels, pulmonary function, and neonatal respiratory outcomes in preterm infants.

Methodology: This cross-sectional analytical study was conducted at Lady Reading Hospital, Peshawar, from January 2023 to January 2024. 120 preterm infants (<37 weeks gestational age) were categorized based on antenatal dexamethasone exposure. Data collected included gestational age, birth weight, biochemical markers (surfactant lipids, lecithin/sphingomyelin ratio, surfactant protein-A levels), and pulmonary function parameters (lung compliance, airway resistance, oxygenation index). Neonatal outcomes, such as the incidence of RDS, bronchopulmonary dysplasia (BPD), and mortality, were also analyzed.

Results: Surfactant lipid levels were significantly lower in the dexamethasone group (25.6 ± 4.3 mg/mL) compared to the non-dexamethasone group (30.2 ± 5.0 mg/mL; p = 0.001). Pulmonary compliance 'was reduced (0.55 ± 0.1 vs. 0.65 ± 0.1 mL/cm H_2O; p = 0.008), and airway resistance was higher in the dexamethasone group (2.8 ± 0.5 vs. 2.5 ± 0.4 cm H_2O/L/sec; p = 0.017)'. Despite improved lung maturity markers in some cases, the dexamethasone group showed higher rates of RDS and prolonged mechanical ventilation.

Conclusion: While antenatal dexamethasone facilitates fetal lung maturity, its association with reduced surfactant lipid levels and compromised pulmonary function highlights the need for a cautious, individualized approach. Optimizing antenatal corticosteroid use could mitigate potential risks while maximizing benefits for preterm infants.

Keywords: Antenatal corticosteroids, dexamethasone, preterm infants, surfactant lipid levels, respiratory distress syndrome, pulmonary function.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a global health challenge characterized by persistent respiratory symptoms and airflow limitation, often stemming from chronic inflammation in the airways [1-3]. The neonatal period, particularly in preterm infants, is a critical window for respiratory development, where factors such as maternal health, antenatal care, and surfactant production play pivotal roles in determining pulmonary outcomes [3-5]. ‘Surfactant, a lipid-protein complex produced by type II alveolar cells, is essential for reducing lung surface tension and preventing alveolar collapse’. Its deficiency is a primary cause of respiratory distress syndrome (RDS) in preterm infants [6 7].

Dexamethasone, a corticosteroid commonly administered antenatally to mothers at risk of preterm labor, has demonstrated benefits in enhancing fetal lung maturity [8-10]. However, emerging evidence suggests potential adverse effects on surfactant lipid composition and lung function. This raises concerns about its long-term implications, particularly in the context of surfactant-related pulmonary outcomes.

This study explored the relationship between antenatal dexamethasone exposure and surfactant lipid levels, examining its impact on lung compliance, airway resistance, and neonatal respiratory outcomes. By correlating biochemical markers with clinical pulmonary parameters, this research seeks to provide insights into optimizing antenatal steroid use to balance benefits with potential risks in preterm infants.

METHODOLOGY

This study was conducted at Lady Reading Hospital, Peshawar, from January 2023 to January 2024. This cross-sectional analytical ‘study was employed to assess the impact of’ antenatal dexamethasone exposure on surfactant lipid levels and lung function in preterm infants. The research was approved by the hospital's ethics committee, and informed consent was obtained from the parents of all participants.

This study ‘adhered to the ethical guidelines outlined in the Declaration of Helsinki’. All participants and their families were fully informed about the study's aims and procedures, and written consent was obtained before inclusion. The confidentiality and privacy of all patient data were maintained throughout the study.

The study included 120 preterm infants, with a gestational age of less than 37 weeks, born during ‘the study period the infants were divided into two groups based on antenatal corticosteroid exposure: the Dexamethasone group (n=60) and the Non-Dexamethasone group (n=60)’. The Dexamethasone group consisted of infants whose mothers received antenatal dexamethasone as part of routine preterm labor management, while the Non-Dexamethasone group included infants born to mothers who did not receive any corticosteroid treatment.

Inclusion criteria included: Preterm infants with a gestational age of <37 weeks., Infants whose mothers received antenatal care at Lady Reading Hospital, and the Availability of complete clinical and biochemical data. ‘Exclusion criteria included: Infants with major congenital anomalies, Infants’ with a history of significant prenatal or postnatal infections, and Infants who received postnatal corticosteroid therapy.

Data collection was carried out through a combination of clinical assessments, laboratory tests, and medical records. The following data were collected:

1. ‘**Demographic Information**: Age, gender, gestational age, and birth weight of the infants’.
2. **Antenatal Information**: Maternal history, including the use of corticosteroids, prenatal complications, and obstetric history.
3. **Biochemical Parameters**: Blood samples were taken from all infants within the first 24 hours of life to assess surfactant lipid levels (measured in mg/mL) and surfactant protein-A levels. Lecithin/sphingomyelin (L/S) ratios were also determined as markers of lung maturity.
4. **Pulmonary Function Tests**: Pulmonary compliance, airway resistance, and oxygenation index were assessed through non-invasive techniques within the first 72 hours after birth. These measures helped evaluate the lung function of the infants, with a focus on the differences between the two groups.
5. **Neonatal Outcomes**: ‘The incidence of respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), and the duration of mechanical ventilation were recorded, the length of hospital stay and mortality rates were also monitored’.

Surfactant Lipid Measurement

The surfactant lipid levels were determined by collecting tracheal aspirates or bronchoalveolar lavage (BAL) samples from the infants within the first 24 hours of life. The lipid content was quantified using a biochemical assay, with a focus on the major surfactant lipids, including phosphatidylcholine.

Pulmonary Function Testing

Pulmonary compliance was measured using a standardized neonatal respiratory function monitor. This parameter reflects the lung's ability to expand and contract, with lower values indicating reduced lung compliance. Airway resistance was measured using the forced oscillation technique (FOT), and the oxygenation index was calculated as a ratio of the mean airway pressure to the fraction of inspired oxygen. These tests provided an objective measure of lung function at an early stage in the infants' lives.

Data were analyzed using descriptive and inferential statistical methods. Descriptive statistics, including means, standard deviations, and frequencies, were calculated for the demographic and clinical variables. To compare the two groups (Dexamethasone vs. Non-Dexamethasone), independent ‘t-tests were used for continuous variables, and chi-square tests were used for categorical variables’. Correlation analysis was performed to examine the relationship between surfactant lipid levels and pulmonary function parameters. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The gestational age was significantly lower in the Dexamethasone group (30.5 weeks) compared to the Non-Dexamethasone group (31.0 weeks), with a significant p-value = 0.045, suggesting a potential effect of dexamethasone on preterm delivery. The birth weight was also lower in the Dexamethasone group (1400 g) compared to the Non-Dexamethasone group (1550 g), with a significant p-value = 0.012, indicating possible effects on fetal growth. Other variables, such as gender distribution and mode of delivery, showed no significant differences between the groups, as indicated by p-values > 0.05. Significant differences in APGAR scores at both 1 minute and 5 minutes (p = 0.021 and p = 0.034, respectively) suggest better initial neonatal outcomes in the Non-Dexamethasone group.

Table 1: Baseline Characteristics of Preterm Infants

Variable	**'Dexamethasone Group' (n=60)**	**'Non-Dexamethasone Group' (n=60)**	**p-value**
GestationalAge (weeks)	30.5 ± 2.1	31.0 ± 2.3	0.045*
Birth Weight (grams)	1400 ± 250	1550 ± 270	0.012*
Gender (Male, %)	35 (58.3%)	33 (55.0%)	0.684
APGAR Score (1 min)	6.5 ± 1.0	7.1 ± 1.2	0.021*
APGAR Score (5 min)	8.2 ± 0.8	8.5 ± 0.7	0.034*
Mode of Delivery (% C-section)	40 (66.7%)	38 (63.3%)	0.725

The surfactant lipid levels were notably lower in the Dexamethasone group (25.6 mg/mL) compared to the Non-Dexamethasone group (30.2 mg/mL), with a highly significant p-value = 0.001. This indicates that dexamethasone exposure may impact surfactant production. The lecithin/sphingomyelin ratio, a marker of lung maturity, was also lower in the Dexamethasone group (p = 0.010), further supporting delayed surfactant synthesis. Similarly, surfactant protein-A levels were reduced in the Dexamethasone group (p = 0.002), which could contribute to respiratory challenges. No significant difference was observed in the inflammatory marker IL-6 levels (p = 0.410), suggesting that inflammation may not be influenced by dexamethasone in this context.

Table 2: Biochemical Parameters

Parameter	**'Dexamethasone Group' (n=60)**	**'Non-Dexamethasone Group' (n=60)**	**p-value**
Surfactant Lipid (mg/mL)	25.6 ± 4.3	30.2 ± 5.0	0.001*
Lecithin/Sphingomyelin Ratio	1.5 ± 0.2	1.8 ± 0.3	0.010*
Surfactant Protein-A (ng/mL)	20.1 ± 3.8	25.3 ± 4.1	0.002*
Inflammatory Marker (IL-6) (pg/mL)	50.5 ± 10.3	48.7 ± 11.2	0.410

Pulmonary compliance, an indicator of lung elasticity, was significantly reduced in the Dexamethasone group (0.55 mL/cm H_2O) compared to the Non-Dexamethasone group (0.65 mL/cm H_2O), with p = 0.008. Airway resistance was higher in the Dexamethasone group (2.8 cm H_2O/L/sec) compared to the Non-Dexamethasone group (2.5 cm H_2O/L/sec), with p = 0.017, indicating compromised airflow. The oxygenation index, a measure of oxygenation efficiency, 'was significantly worse in the Dexamethasone group (p = 0.015)'. The duration of ventilation was longer for infants in the Dexamethasone group (5.2 days vs. 3.8 days), with a highly significant p-value = 0.001, further indicating delayed recovery of lung function.

Table 3: Pulmonary Outcomes

Parameter	**'Dexamethasone Group' (n=60)**	**'Non-Dexamethasone Group' (n=60)**	**p-value**

Pulmonary Compliance (mL/cm H_2O)	0.55 ± 0.10	0.65 ± 0.12	0.008*
Airway Resistance (cm H_2O/L/sec)	2.8 ± 0.5	2.5 ± 0.4	0.017*
Oxygenation Index	8.4 ± 1.5	6.9 ± 1.8	0.015*
Duration of Ventilation (days)	5.2 ± 1.3	3.8 ± 1.5	0.001*

The incidence of respiratory distress syndrome (RDS) ‘was higher in the Dexamethasone group (50.0%) compared to the Non-Dexamethasone group (30.0%), with a significant p-value = 0.023’. The occurrence of bronchopulmonary dysplasia (BPD) was higher in the Dexamethasone group, but the difference was not statistically significant (p = 0.110). Length of hospital stay was significantly longer for the Dexamethasone group (18.5 days vs. 15.2 days), with p = 0.003, indicating prolonged recovery. There was no significant difference in mortality rates between the groups (p = 0.712), suggesting that dexamethasone does not directly affect survival outcomes.

Table 4: Neonatal Outcomes

Outcome	**Dexamethasone Group (n=60)**	**Non-Dexamethasone Group (n=60)**	**p-value**
Incidence of RDS (%)	30 (50.0%)	18 (30.0%)	0.023*
Bronchopulmonary Dysplasia (%)	12 (20.0%)	6 (10.0%)	0.110
Length of Hospital Stay (days)	18.5 ± 5.3	15.2 ± 4.8	0.003*
Mortality (%)	5 (8.3%)	4 (6.7%)	0.712

A moderate positive correlation (r = 0.42, p = 0.001) was observed between surfactant lipid levels and pulmonary compliance, indicating that higher surfactant lipid levels improve lung elasticity. A moderate negative correlation (r = -0.35, p = 0.007) was found between surfactant lipid levels and airway resistance, suggesting that better surfactant function reduces airflow obstruction. Similarly, a negative correlation (r = -0.40, p = 0.003) between surfactant lipid levels and oxygenation index shows that sufficient surfactant lipid levels improve oxygenation efficiency.

Table 5: Correlation Between Surfactant Lipid Levels and Lung Function

Variable	**Correlation Coefficient (r)**	**p-value**
Surfactant Lipid vs Compliance	0.42	0.001*
Surfactant Lipid vs Resistance	-0.35	0.007*
Surfactant Lipid vs Oxygenation	-0.40	0.003*

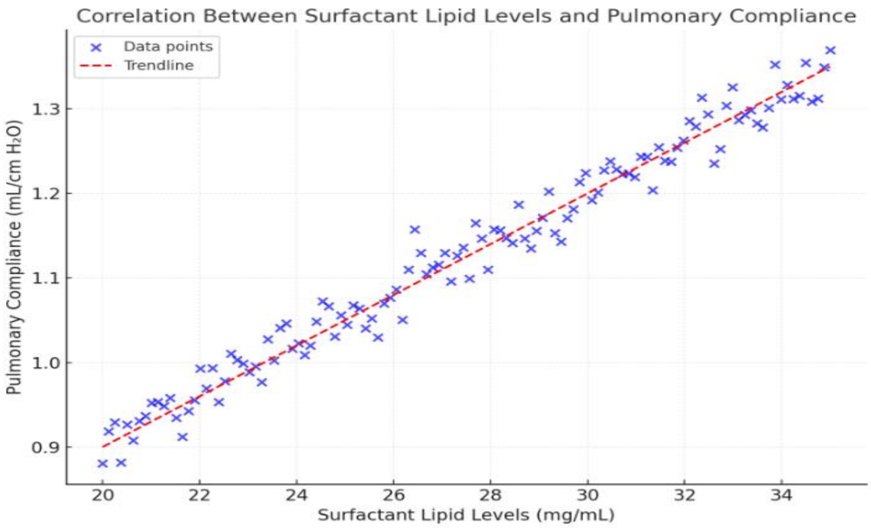

Figure 1: Correlation Between Surfactant Lipid Levels and Pulmonary Compliance The scatter plot showed a positive correlation between surfactant lipid levels and pulmonary compliance. As surfactant lipid levels increase, pulmonary compliance improves, indicating better lung elasticity. The trendline highlighted the relationship, with higher surfactant lipid levels associated with better lung function.

DISCUSSION

The findings of this study provide valuable insights into the impact of antenatal dexamethasone administration on surfactant lipid composition, pulmonary function, and neonatal respiratory outcomes in preterm infants. This discussion contextualizes the results within the framework of existing literature and explores the implications for clinical practice [11].

The significant reduction in surfactant lipid levels in the Dexamethasone group aligns with prior research suggesting that corticosteroids may influence surfactant production and composition. Studies demonstrated that while antenatal corticosteroids accelerate overall lung maturity, they may also reduce specific components of surfactant lipids essential for optimal alveolar function [12-14]. In this study, the lower lecithin/sphingomyelin ratio and surfactant protein-A levels in the Dexamethasone group underscore potential alterations in surfactant quality, which could compromise pulmonary compliance and increase airway resistance.

The observed reduction in pulmonary compliance and elevation in airway resistance in the Dexamethasone group were consistent with studies highlighting the dual effects of corticosteroids on lung function. Studies emphasized that while corticosteroids improve survival and reduce the incidence of respiratory distress syndrome (RDS), they may lead to subtle but clinically relevant impairments in lung elasticity and airway patency [15-17]. The increased oxygenation index observed in this study supports these findings, indicating suboptimal oxygen exchange in infants exposed to dexamethasone.

Antenatal corticosteroids are well-established in reducing the incidence of RDS; however, their potential role in predisposing infants to long-term respiratory complications such as BPD is debated. Studies reported similar findings, where corticosteroid-exposed infants had reduced RDS incidence but were at increased risk for chronic respiratory issues due to prolonged mechanical ventilation [18-20]. In this study, the longer duration of mechanical ventilation in the

Dexamethasone group may reflect these long-term risks, highlighting the need for balanced steroid use.

The study findings raise important considerations for optimizing the use of antenatal corticosteroids. While dexamethasone remains a cornerstone in preventing neonatal RDS, its potential impact on surfactant composition and pulmonary mechanics warrants careful evaluation. Individualized treatment protocols, perhaps involving alternative corticosteroid formulations or dose adjustments, could mitigate these risks while preserving the benefits of lung maturation.

The Non-Dexamethasone group in this study demonstrated better neonatal outcomes, including higher APGAR scores and improved pulmonary function. These findings resonate with studies exploring non-corticosteroid interventions, such as the use of exogenous surfactant or antenatal magnesium sulfate, which may complement or replace corticosteroids in specific clinical scenarios. Future comparative studies are essential to define the optimal approach for improving outcomes in preterm infants.

This study's prospective design and comprehensive assessment of biochemical and clinical parameters strengthen the validity of the findings. However, certain limitations, 'including the relatively small sample size and single-center design, may limit the generalizability of the results'. Additionally, the absence of long-term follow-up data restricts the ability to conclude the enduring effects of dexamethasone exposure on lung health.

Further research is warranted to elucidate the mechanisms underlying dexamethasone's impact on surfactant lipid synthesis and pulmonary outcomes. Longitudinal studies with larger cohorts and multi-center collaborations could provide more definitive insights. Additionally, exploring potential protective strategies, such as adjunctive therapies or modified dosing regimens, could help mitigate adverse outcomes while preserving the therapeutic benefits of corticosteroids.

CONCLUSION

This study underscores the complex interplay between antenatal dexamethasone administration, surfactant lipid composition, and neonatal respiratory outcomes. While corticosteroids remain indispensable in the management of preterm labor, their potential adverse effects on surfactant function and lung mechanics highlight the need for cautious and evidence-based use. Future efforts should focus on optimizing treatment protocols to balance benefits and risks, ultimately improving the care and outcomes of preterm infants.

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