Original Article

Short Term Outcomes of the Use of Antenatal Steroids in Preterm Infants

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ABSTRACT

Objective: To compare the short-term outcome of antenatal exposure to steroids in the case of planned and unplanned antenatal steroids.

Study Design: A **r**etrospective study

Place and Duration of Study: This study was conducted at the Neonatology Department of Recep Tayyip Erdogan Hospital Muzaffargarh between July 2016 till June 2021.

Materials and Methods: The cases of mothers who were at risk of preterm labor were given 12 mg dexamethasone 24 hours apart and then followed for the next seven days to determine the frequency of pregnancies delivered during the effective period of steroid, i.e., 24 hrs. after and within seven days of the last dose of steroid and then divided in two groups A and B. Group A included those who received Planned steroids and Group B included those who received Unplanned steroids. Data were compared between the two groups.

Results: Out of 201 preterm neonates, 140 (69.7%) were administered planned steroids. A total of 44 (21.89%) suffered from respiratory distress syndrome (RDS), 13 (6.47%) from retinopathy of prematurity, 11 (5.47%) from necrotizing enterocolitis, and 8 (3.98%) from pneumothorax. 8 (3.98%) preterm babies expired. Lower weight and gestational age were significantly associated with a higher rate of mortality ($p<0.0001$).

Conclusion: Patients with planned steroid administration suffered from significantly lower rates of neonatal complications than those with unplanned antenatal steroid administration.

Key Words: Antenatal Corticosteroids, Intraventricular Hemorrhage, Necrotizing Enterocolitis, Premature Birth, Respiratory Distress Syndrome, Retinopathy of Prematurity

Citation of article: Shabeer MR, Razzaq A, Ahmad E, Ali M, Arshad S, Abbas K. Short Term Outcomes of the Use of Antenatal Steroids in Preterm Infants. Med Forum 2022;33(8):64-68.

INTRODUCTION

Premature birth is a global anathema. [1] Its incidence is 7 to 12 % in developed countries,[2] while in Pakistan it is 21%. Death due to premature birth ranks second overall (28%).[1] Death from respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and retinopathy of prematurity (ROP), as well as premature birth's overall mortality rate, are all higher in premature infants. Complications of prematurity can be avoided by using antenatal steroids between 24 to 37 weeks of gestation.[3] In 1972, Sir Graham Collingwood Liggins with Ross Hawie became the first to legally sell anabolic steroids.[3-5]

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Received: March, 2022
Accepted: May, 2022
Printed: August, 2022

Antenatal steroids administration reduces admission to NICU, duration of hospital stay, financial burden, parental anxiety, separation of the newborn from the mother, and Increased risk of morbidity due to secondary infection acquired during the hospital stay. [4] Antenatal steroids reduce respiratory morbidity via different mechanisms. [1] By increasing the number and function of the Sodium channel in the apical membrane of the respiratory epithelium.[2] Increasing responsiveness to catecholamines and thyroid hormones. Steroids should be given to all women for whom a C-section is planned before 37 weeks.[3] Betamethasone and Dexamethasone are the most commonly used steroids.[6-9]

Antenatal corticosteroids have been shown to have deleterious impacts on the health, with no observable changes in the Doppler waveform sequences of fetoplacental arteries, but rather a decrease in i) fetal body, ii) fetal breathing movements, and iii) fetal heart rate variation. Multiple doses of corticosteroids given before delivery have been linked to decreased fetal growth inside the womb and lower birth weight babies. Neonatal sepsis can occur more quickly if the baby has been given steroids several times.[9-12]

Antenatal steroids are practiced and discussed worldwide a lot in the last decade or so, but up to our knowledge published data is insufficient. We have established gynae and neonatology units and have a

large amount of saved data regarding the use of antenatal steroids. We want to share and discuss our data and experience across the country and worldwide. The present study aimed to compare the short-term outcome of antenatal exposure to steroids in the case of planned and unplanned groups in terms of mortality and morbidity in neonates.

MATERIALS AND METHODS

A **r**etrospective study was conducted at the Neonatology department of Recep Tayyip Erdogan hospital Muzaffargarh and data of newborns who were delivered between 24 to 37 weeks of gestation from 1st July 2016 till 30th June 2021 were assessed after the ethical committee's exemption was approved.

Records were retrieved for all those neonates whose mothers had received antenatal steroids between 24 and 37 weeks of gestation were included in the study while all those neonates who were dysmorphic, hypoxic encephalopathy grade 3, complex congenital heart diseases, surgical anomalies were excluded.

The primary outcome of the study was the mortality rate and its association with the sociodemographic and antenatal parameters. The frequencies of respiratory distress syndrome (RDS), pneumothorax, necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), and retinopathy of prematurity were secondary outcomes.

Planned steroid was described as delivery conducted 24 hours after and within seven days of administration of 2nd dose of steroids.[15] Unplanned Steroid was described as delivery conducted less than 24 hours before 2nd dose and after seven days of the last dose of steroid.[15]

For the diagnosis of RDS, the patients must be a preterm neonate, suffer from respiratory difficulty within the first six hours of life, and lack lung expansion on skiagram; air bronchogram; reticulogranular pattern; ground-glass opacity.[8]

Pneumothorax was defined as air getting into the pleural space. [6] NEC was diagnosed upon radiographic proof of intestinal pneumatosis, pleural effusion, or subdiaphragmatic free air. [8]

IVH was diagnosed when preterm infants exhibited any three of the clinical criteria;

- Symptoms that appear within 0-72 hours of age
- Apneic episodes or convulsions
- Abrupt pallor or dropping hematocrit
- Profound hypotonia
- Confirmation of a flat or protruding fontanel via ultrasound, CT, or autopsy.[8]

Retinopathy of prematurity (ROP) preterm infants often develop a condition of the eye called retinopathy of prematurity, which is caused by the abnormal development of blood vessels in the retina. Infants born before the 31st week of pregnancy and weighing less than 2.75 pounds (1,250 grammes) are at increased risk for developing retinopathy of prematurity.[8]

Recep Tayyip Hospital, Muzaffargarh Neonatology Department comprises 25 neonatal beds delivering level III neonatal services to 10 and level II to 10 neonates. This institute uses HIMS for patient data. Our sample consisted of mothers whose newborns were admitted to the NICU and who used steroids throughout pregnancy, from 1st July 2016 till 30th June 2021. Those mothers who were at risk of preterm labor were given 12 mg dexamethasone 24 hours apart and then followed for the next seven days to determine the frequency of pregnancies delivered during the effective period of steroid, i.e., 24 hrs. after and within seven days of the last dose of steroid and then divided in two groups A and B.

Group A: Those who received Planned steroids

Group B: Those who received Unplanned steroids

We compared neonates of group A and B with respect to the short-term neonatal outcomes. We analyzed the data by using SPSS version 26. Frequencies and percentages of categorical variables (like gender, mortality) were reported. Mean (SD) or median (interquartile range) for numerical data (like weight, duration of respiratory support like oxygen, CPAP, Invasive ventilation). Chi-square test was applied to see the association of gender, mortality and other categorical variables with planned and unplanned steroids. A p-value less than 0.05 was considered statistically significant.

RESULTS

Table No.1: Demographic and Natal Characteristics of Study Subjects

Weight (grams)	2307.01 ± 465.7
Gestational age (weeks)	35.7 ± 2.3
Duration of hospital stay (days)	2.69 ± 3.8
Gender	
Female	95 (47.3%)
Male	106 (52.7%)
Mode of delivery	
Cesarean Section	153 (76.1%)
Spontaneous vaginal delivery (SVD)	48 (23.9%)
Planned steroid given	140 (69.7%)
Unplanned steroids given	54 (26.9%)
Duration of rupture of membrane >18 hrs	24 (11.9%)
Birth at own hospital	197 (98%)
Birth attended by trained personnel	198 (98.5%)
Stay at other hospital for >48 hours (out born)	161 (80.1%)

A total of 201 preterm neonates were assessed with a mean gestational age of 35.7 ± 2.3 months and a mean weight of 2307.01 ± 465.7 grams. 153 (76.1%) of the

mothers delivered via cesarean. 140 (69.7%) were administered planned steroids (Table 1).

In our study, 27 (13.4%) needed active resuscitation at the time of delivery and 47 (23.4%) required respiratory support during the hospital stay. 11 (5.47%) neonates were on invasive ventilation for 1-3 days, while 8 (3.98%) patients were ventilated for longer than three days. Moreover, cultures were positive for 25 (12.44%) patients, and 44 (21.89%) neonates were started on intravenous antibiotics.

A total of 44 (21.89%) suffered from respiratory distress syndrome (RDS), 13 (6.47%) from retinopathy of prematurity, 11 (5.47%) from necrotizing enterocolitis, and 8 (3.98%) from pneumothorax. 8 (3.98%) preterm babies expired. Neonates with a lower weight and a lower gestational age had significantly higher rates of RDS, intraventricular hemorrhage, necrotizing enterocolitis, and pneumothorax ($p<0.0001$). Neonates with longer duration of CPAP had significantly higher frequency of RDS, intraventricular hemorrhage, necrotizing enterocolitis, pneumothorax, and retinopathy of prematurity ($p<0.05$). RDS, intraventricular hemorrhage, necrotizing enterocolitis, pneumothorax, and retinopathy of prematurity were correlated with significantly longer duration of oxygen mask, invasive ventilation, and hospital stay ($p<0.05$).

Lower weight and gestational age were significantly associated with a higher rate of mortality ($p<0.0001$). Patients who expired had significantly longer duration of CPAP and invasive ventilation than those who survived. Gender and mode of delivery did not significantly correlate with mortality. Seven (87.5%) patients who had unplanned administration of steroids expired ($p<0.0001$) as illustrated in Table 2.

Table No.2: Association between subject characteristics and Mortality

	Mortality		
	No	**Yes**	**p-value**
Weight (grams)	2343.05 ± 428.8	1437.5 ± 504.09	<0.0001
Gestational age (weeks)	35.9 ± 2.048	30.88 ± 2.8	<0.0001
Duration of CPAP (days)	0.55 ± 1.266	1.5 ± 1.414	0.041
Duration of oxygen mask (days)	0.3 ± 0.656	0.75 ± 1.389	0.074
Duration of invasive ventilation (days)	0.19 ± 0.801	3.38 ± 1.061	<0.0001
Duration of hospital stay (in days)	2.56 ± 3.809	5.75 ± 2.915	0.021
Gender			0.378
Female	90 (46.6%)	5 (62.5%)	
Male	103 (53.4%)	3 (37.5%)	
Mode of delivery			0.106
Cesarean Section	145 (75.1%)	8 (100%)	
Spontaneous vaginal delivery (SVD)	48 (24.9%)	0 (0%)	
Planned steroid given	139 (72%)	1 (12.5%)	<0.0001
Unplanned steroid given	47 (24.4%)	7 (87.5%)	<0.0001

DISCUSSION

The present study revealed that patients with planned steroid administration suffered from significantly lower rates of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), pneumothorax, and mortality compared to those with unplanned antenatal steroid administration.

Our study was in accordance with published literature. Amorim et al., revealed the incidence of respiratory distress syndrome of 23%; lower in the steroid group compared to the placebo group. The rate of neonatal deaths was lower in the corticosteroid group (14% vs. 21%). In patients with severe preeclampsia between 26 and 34 weeks of gestation, antenatal corticosteroid therapy with betamethasone to accelerate fetal lung maturity is a safe and effective treatment. [16]

The positive effect of prenatal corticosteroids on RDS in clinical settings is further confirmed by the findings of a research by Eriksson et al. The risk of Sudden Infant Death Syndrome, late neonatal death, bronchopulmonary dysplasia, respiratory distress syndrome, intraventricular hemorrhage, and cerebral palsy was lower in exposed newborns after adjusting for confounding factors.[17] An antenatal steroid birth interval of 24 hours to seven days is highly related with a decreased risk of intraventricular hemorrhage in extremely low birth weight infants, according to a study by Fortmann et al.[18] As per another study, antenatal steroid administration decreases neonatal mortality in infants delivered at gestation < 37 weeks.[19] In addition, evidence from Wang et al. suggests that ACS decreases the requirement for endotracheal tube placement and the use of exogenous surfactant in very low birth weight (VLBW) preterm newborns. Multiple-dose ACS newborns were less likely to receive surfactant and had a lower rate of intubation compared to their non-ACS counterparts. Intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, sepsis, and

chronic lung disease all occurred at the same rates regardless of whether the infant received a single dosage of ACS or many doses, or if they were given betamethasone or dexamethasone.[20]

On a contrary, a study by Porto et al. suggests that the incidence of respiratory disorders is not affected by antenatal administration of steroids after 34 weeks' gestation. Antenatal treatment with corticosteroids at 34-36 weeks of pregnancy does not reduce the incidence of respiratory disorders in newborn infants.[21] Bonanno et al also concluded that antenatal corticosteroids have proven effective for singleton pregnancies at risk for preterm birth between 26 and 34 weeks gestation, questions remain about the utility in specific patient populations such as multiple gestations, very early preterm gestations, and pregnancies complicated by intrauterine growth restriction.[5]

CONCLUSION

The present study revealed that patients with planned steroid administration suffered from significantly lower rates of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), pneumothorax, and mortality compared to those with unplanned antenatal steroid administration.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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