Antenatal Corticosteroids in Elective Term Cesarean Swction

Original Article

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ABSTRACT

Background: Antenatal corticosteroid is a best documented treatment for enhancing fetal lung maturity before 34 weeks however, there is no enough evidence for its use after 34 weeks.

Objective: To assess the effect of prophylactic corticosteroid administration before elective caesarean section at term (after completed 37 weeks), in reducing neonatal respiratory morbidity.

Patients and Method: This is a double-blinded randomized controlled trial during the period from February 2018 till August 2020 to assess the role of prophylactic dexamethasone administration given in dose of 6mg, 4 doses 12 hours apart 48 hours before elective caesarean section at term. 500 women were included in this study. Participants were randomly divided into two groups; Group I (250 women) who received prophylactic dexamethasone and group II (250 women) who received a placebo.

Results: NICU admission was significantly lower in Group I compared to placebo [8 (3.2%) vs. 17 (6.8%), respectively] (P= 0.049). Also, group I had better APGAR score than group II at 1 and 5min, (p<0.001). There were no significant differences between both groups regarding maternal and other adverse neonatal events.

Conclusion: Antenatal corticosteroids may be effective in reducing respiratory complications in neonates delivered by elective caesarean section at term.

Key Words: Antenatal, corticosteroids, elective term cesarean section.

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INTRODUCTION

Respiratory distress syndrome (RDS) is one of the most important causes of early neonatal morbidity and mortality[1].

ANCS before preterm delivery is one of the best documented and most cost effective lifesaving treatments in prenatal medicine[2]. The rate of term infants born by cesarean section is increasing globally[3]. Infants born at term by elective caesarean delivery are more likely to develop respiratory morbidity than infants born vaginally[4].

Elective caesarean section compared with intended vaginal delivery leads to a twofold to fourfold increased risk of overall neonatal respiratory morbidity and even higher relative risks of serious respiratory morbidity in term newborns.

The risk of respiratory complications, mostly respiratory distress syndrome and transient tachypnea, decreases from 37 weeks to 39 weeks of gestation, at which stage it is low. Antenatal corticosteroids use has been shown to reduce the risk of respiratory problems in infants born before 34 weeks[4].

However, approximately 10% to 15% of women planned for caesarean may deliver before 39 weeks, and there may be concerns about waiting in the presence of specific clinical indications or previous history. Prophylactic corticosteroids in singleton preterm pregnancies accelerate lung maturation and reduce the incidence of RDS, and administration of steroids is currently recommended between 24 and 34 weeks in cases of threatened preterm labor, antepartum hemorrhage, preterm rupture of membranes or in any condition requiring elective preterm delivery[5-7].

The objective of this study was to assess the effect of prophylactic corticosteroid administration before elective caesarean section at term (after 37 completed weeks), in reducing neonatal respiratory morbidity and admission to special care units with respiratory complications.

PATIENTS AND METHODS

This is a double-blinded randomized controlled trials by random allocation, which was conducted at the Woman

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Health Hospital, Assiut University and Dairout hospital during the period from February 2018 till August 2020 to assess the role of prophylactic antenatal dexamethasone administration given before elective caesarean section at full term. The Clinical trial gov number is NCT03396107.

Sample size calculation:

Using G*Power 3 software (13). A calculated minimum sample of 495 (raised to 500) pregnant women candidate for elective CS (randomly assigned into one of two equal groups (1:1) ANCS (Group1) or control (Group2)) was needed to detect an effect size of 0.2(14) in the reduction of neonatal respiratory morbidity, with an error probability of 0.05 and 95% power on a two-tailed test.

Unblinded researchers were designated at the start of the trial, including unblinded pharmacist and investigators, and they will not participate in the subsequent process of data management and data analysis. The unblended researchers will prepare the antenatal corticosteroids or placebo according to the treatment assignment. Neither the enrolled pregnant women nor the other investigators will be aware of the result of random assignment.

Participants:

Inclusion criteria were women aged 18-35 years, singleton pregnancy, 37-41 weeks gestation, delivered by elective cesarean section.

Women with major comorbidities as pregestational DM, severe pre-eclampsia, bronchial asthma, heart diseases, major congenital anomalies affecting neonatal survival, IUGR, marked oligohydramnios, antepartum hemorrhage, preterm labor, multiple pregnancies, and women who received corticosteroids during pregnancy were excluded.

Women assessed for eligibility criteria were 683, 133 cases were excluded, 28 delivered normally, 33 developed pre-eclampsia and 16 IUFD.

Randomization was done to the remaining 550 cases into two groups, group1 (Dexamethasone) (*n*= 280) and group 2 (control) (*n*= 270), after randomization we exclude 30 cases from group 1 and 20 cases from group 2 which was lost to follow up.

Group I (Dexamethasone group *n*= 250) received intramuscular dexamethasone 6mg, 12 hours apart, 48 hours before performing the CS, while Group II (control group *n*= 250) received saline (as a placebo) (Figure 1).

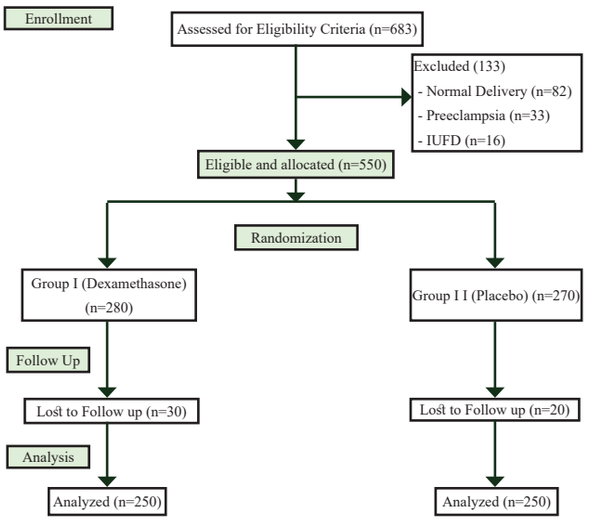

Fig. 1: Flow Chart of the studied Cohort.

Cesarean section was done to all cases by lower segment cesarean section according to ACOG guidelines, this was done by obstetrician.

An approval of the study was obtained from Assiut University academic and ethical committee.

Women were approached, provided all necessary information and counseled as regards trial participation by the co-investigator or care provider. Written informed consent was obtained from every participant.

This trial approved by IRB of Assiut university no 17101493.

Statistical Methods:

The collected data will be verified, coded by the researcher, and analyzed using the Statistical Package for Social Sciences (IBM-SPSS/PC/VER 24) (15). Descriptive statistics: continuous variables were expressed as mean ± standard deviation, median, range, and qualitative data was expressed as frequencies and percentage. Test of significances: Chi-square/Fisher's exact/Monte Carlo exact test was used to compare the difference in distribution of frequencies among different groups as appropriate. The Shapiro-Wilk test was used to test data normality. Student *t*-test/ Mann-Whitney *U* test was calculated to test the differences in mean/median of continuous variables between groups (parametric/non-parametric) as appropriate. Significant test results were considered when *p value* was <0.05.

RESULTS

There was non-significant difference between the studied groups regarding the socio-demographic and obstetric data as shown in (Table 1).

Likewise, the two studied groups were comparable regarding the operative data and there was no significant difference between both groups (Table 2).

Moreover, there was non-significant difference between both groups regarding neonatal birthweight, however, the majority of neonates were born within normal range of birthweight (Table 3). Regarding other adverse neonatal outcome, there was no significant difference between two groups in neonatal RDS, need for mechanical ventilation, neonatal mortality, oxygen supplementation, need for CPAP, need for surfactant, anemia and neonatal sepsis (Table 4).

On the other hand, respecting the neonatal APGAR score, there was significant difference between the two groups either at 1 minute or at 5 minutes i.e., group I cases having better APGAR score at 1-min. ≤7 were 21(8.4%) vs.36(14.4%), *p*= 0.035 and APGAR at 5-min. ≤ 7 were 16 (6.4%)vs. 42(16.8%), *p*= 0.001 (Table 3). Likewise, the rate of admission to NICU was significantly lower in group I when compared to group II (3.2% (*n*= 8) vs. 6.8% (*n*= 17), respectively with significant difference (*P*= 0.049) (Table 4).

Table 1: Baseline Demographic/Clinical and Obstetric Data of the studied groups:

	Treatment Group *n*=250)	Control Group *n*=250)	*P*. value
Age (in years)			
• Mean±SD	31.61 ± 6.7	30.60±5.9	0.073 NS
• Median (Range)	33 (20 – 40)	29(20–40)	
Parity			
• Mean±SD	1.85 ± 1.5	1.68±1.3	0.266 NS
• Median (Range)	2 (0 – 5)	1(0–5)	
BMI (kg/m²)			
• <18.5(underweight)	11(4.4%)	12(4.8%)	
• 18.5–24.9(normal)	165(66%)	175(70%)	0.712 NS
• 25–29.5(overweight)	53(21.2%)	47(18.8%)	
• ≥ 30 (Obese)	21(8.4%)	16(6.4%)	
Previous CS(0-4)			
• Mean±SD	2±1	2±2	1.000 NS
• Median (Range)	2(1–4)	2(0–4)	
Gestational age (in weeks)			
• Mean±SD	38.87±1.1	38.76±1.1	0.243 NS
• Median (Range)	38(37–40)	38(37–40)	

*NS= non-significant

Table 2: Difference between two groups according to operative data:

	Treatment Group (*n*=250)		Control Group (*n*=250)		*P*. value
	No.	%	No.	%	
Type of Anesthesia					
• General	46	18.4	54	21.6	0.371 NS
• Spinal	204	81.6	196	78.4	0.371 NS
Amount of Blood Loss (cc)					
• <100 cc	150	60	128	51.2	
• 100–300 cc	55	22	65	26	0.136 NS
• > 300 cc	45	18	57	22.8	
Time from Uterine incision to baby delivery					
≤2min	195	78.0	192	76.8	0.831 NS
> 2min	55	22.0	58	23.2	

*NS= non-significant

Table 3: Neonatal outcome among the studied groups:

	Treatment Group (*n*=250)		Control Group (*n*=250)		*P*-value
	No.	No.	%	No.	
Birth Weight (g)					
• <2500gm	61	24.4	58	23.2	
• 2500–4000 gm	174	69.6	185	74	0.190 NS
• > 4000gm	15	6.0	7	2.8	
1-min Apgar Score					
• ≤7	21	8.4	36	14.4	= 0.035 S
• > 7	229	91.6	214	85.6	
5-min Apgar Score					
• ≤7	16	6.4	42	16.8	<0.001 S
• > 7	234	93.6	208	83.2	

*NS=non-significant.

Table 4: Adverse neonatal outcomes among the studied groups:

	Treatment Group (*n*=250)		Control Group (*n*=250)		*P*-value
	No.	No.	%	No.	
Admission to NICU due to Respiratory and Non-Respiratory Causes					
	8	3.2	17	6.8	0.049 SS
TTN	3	1.2	9	3.6	0.071 NS
Neonatal RDS	2	0.8	4	1.6	0.343 NS
Need for mechanical ventilation					
	2	0.8	5	2	0.225 NS
Neonatal mortality	1	0.4	2	0.8	1.000 NS
Admission to NICU due to jaundice					
	4	1.6	10	4	0.104 NS
Oxygen supplementation	5	2.0	8	3.2	0.288 NS
Need for CPAP	2	0.8	3	1.2	0.501 NS
Anemia	5	2.0	6	2.4	0.501 NS
Neonatal sepsis	1	0.4	1	0.4	1.000 NS

*SS=Statistically Significant **NS=non-significant.

DISCUSSION

Infants born at term by elective cesarean section are more likely to develop respiratory morbidity than infants born vaginally[8].

This study demonstrated a correlation between antenatal corticosteroid use before elective cesarean section and decreasing the rate of neonatal respiratory morbidity especially admission to NICU.

We found that there was statistically significant difference between dexamethasone group and control group regarding admission to NICU 3.2% vs.6.8% respectively *p*= 0.049.

A study conducted at 2018 on 4000 women demonstrated that prophylactic administration of antenatal dexamethasone before elective cesarean section at term reduced the rate of RDS, TTN and NICU admission by approximately 50%[9].

We assumed that this difference was due to larger sample size in the previous study and the group participants which were mostly near 37 weeks (37wk-37wk+6 days), while our study included variable age groups (37 wk-40wk).

Another study conducted at 2005 using prophylactic antenatal betamethasone before elective cs at term reduce the rate of admission to NICU for respiratory complications and this agree with our results, On the other hand there was a reduction in the rate of TTN by 50%[10] unlike our study that demonstrated no significant difference between both

groups , these results in this study was due to larger sample size, around one thousand women or betamethasone may be superior to dexamethasone.

Both dexamethasone and betamethasone are used for lung maturity enhancement in preterm labor.

There were two studies conducted at 2005 and 2007 showed that antenatal dexamethasone was associated with a significantly lower risk of neonatal intraventricular hemorrhage(IVH) than betamethasone (3.5% vs 6,9%) but no significant difference regarding neonatal respiratory problems[11,12].

The generalizability of ANCS use may be limited by drug dose limit and time limit (48 hours) before delivery this may conflict with some cases as patients who come in labor, patients developing pre-eclamptic toxemia and any emergent maternal disease that require urgent termination of pregnancy before completing corticosteroid doses.

In addition, further trials on the long-term neonatal effect of ANCS are needed to identify any potential harms and complications of this regimen before elective term CS.

Finally, it may be better to use ANCS 48 hours before elective cesarean section at term to reduce the rate of admission to NICU for respiratory problems.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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