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Original Research

Effect of Antenatal Corticosteroids in Late Preterm Delivery on Neonatal Respiratory Morbidity: A Randomized Controlled Trial

***Anisah Yahya[1], Hajaratu Umar Sulayman [1], Isa Abdulkadir [2], Bola Biliaminu Lawal[3]**

[1]Department of Obstetrics and Gynecology, College of Medical Sciences, Ahmadu Bello University/Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. [2] Department of Paediatrics, College of Medical Sciences, Ahmadu Bello University/Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. [3] Department of Community Medicine, College of Medical Sciences, Ahmadu Bello University Zaria, Nigeria.

Abstract

Background: The use of antenatal corticosteroids beyond 34 weeks of gestation to prevent certain neonatal complications remains a debate. This study sought to determine the effect of the use of antenatal corticosteroids in late preterm delivery on neonatal morbidity.

Methodology: It was a randomized double-blind placebo and active-controlled multi-arm trial. There were two study groups and one control group. It was conducted at the Department of Obstetrics and Gynaecology and the Department of Paediatrics of Ahmadu Bello University Teaching Hospital Zaria, Nigeria. Pregnant women at 34 weeks to 36 weeks 6 days of gestation scheduled for elective delivery or who had emergency delivery were recruited for the study.

The first study group had 2 doses of 12mg intramuscular dexamethasone and the second study group had 2 doses of 12mg betamethasone. The control group had 2 doses of a placebo. The primary outcome was the incidence of respiratory distress syndrome evidenced by tachypnoea with grunting, recession, or nasal flaring with diffuse reticulogranular infiltrate on X-ray or respiratory distress requiring the need for respiratory support by 72 hours of age. Secondary outcome measures included the need for neonatal resuscitation at birth, admission into the Special Care Baby Unit/Neonatal Intensive Care Unit, transient tachypnoea of the newborn, and apnoea.

Results: A total of 138 mothers and 146 preterm neonates were included. A pairwise analysis was done to test for differences between the groups. There was no difference in the incidence of respiratory distress syndrome between the groups. However, the need for neonatal resuscitation was significantly higher (RR: 7.0; CI: 2.49-19.4; p = <0.001) in the placebo group when compared to the betamethasone group and also significantly higher (RR:4.0; CI: 1.86-26.03; p= 0.01) in the placebo group when compared to the dexamethasone group.

Conclusion: Antenatal corticosteroids may decrease the need for neonatal resuscitation at birth in late preterm neonates.

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Trial registration: ClinicalTrial.gov, NCT03446937

Keywords: Antenatal Corticosteroids, Late Preterm Delivery, Neonatal Morbidity.

***Correspondence:** Anisah Yahya. Department of Obstetrics and Gynecology, College of Medical Sciences, Ahmadu Bello University/Ahmadu Bello University Teaching Hospital, Zaria, Nigeria **Email**: ayahya@abu.edu.ng

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Quick Response Code:

Introduction

Preterm birth is a significant cause of neonatal morbidity and mortality. The use of antenatal corticosteroids before 34 weeks of gestation has been proven to prevent respiratory distress syndrome and other morbidities in neonates. [1] However, limited evidence is available for its use in the late preterm period. [2, 3]

Respiratory distress syndrome is one of the most important causes of neonatal morbidity and mortality in preterm births. Other causes of neonatal morbidity and mortality in preterm neonates include intraventricular haemorrhage, sepsis, periventricular leucomalacia, and necrotizing enterocolitis. In preterm neonates, surfactant insufficiency, immaturity, and poor lung development result in respiratory distress in preterm infants. As gestation advances, chances of survival improve due to the increasing maturity of the respiratory system. Even though black neonates are said to have lower rates of respiratory distress syndrome compared to non-black neonates, [4] most studies on respiratory distress syndrome and other neonatal morbidities in the late preterm period did not involve black neonates. [5]

Even though adequate fetal lung maturation for survival is expected to be achieved by 34 weeks of gestation, neonatal and childhood complications are still common in preterm neonates delivered after 34 weeks of gestation when compared to those delivered at term. [6, 7]This led to the recommendation by the National Institute Of Child Health And Human Development during a workshop in 2005 to direct research to evaluate infants who are born between 34- and 36 weeks gestation, especially with regard to the benefits of the use of antenatal corticosteroids in the population. [8]

This study sought to determine the effect of antenatal corticosteroids on neonatal respiratory distress syndrome and other neonatal complications in women at risk of late preterm delivery in our clinical setting.

Material and methods

Trial Design

The study was a randomized double-blind placebo and actively controlled multi-arm trial. Pregnant women at risk of late preterm delivery or scheduled for delivery in the late preterm period were categorized into three groups. There were two study groups and one control group.

Participants

Pregnant women at 34 weeks 0 days to 36 weeks 6 days of gestation and a probability of delivery in the late preterm period irrespective of diagnosis including women with medical conditions were recruited for the study. Probability of delivery is defined as the presence of uterine contractions and cervical effacement of ≥ 80%, preterm labor which was defined as uterine contractions and cervical dilatation of 3cm, and premature rupture of membranes which was defined as evidence of liquor drainage by the bedside.

Also, pregnant women scheduled for delivery in the late preterm period irrespective of indication and route of delivery were recruited.

Women with unsure date, chorioamnionitis, foetal distress, and foetal congenital anomalies were excluded from the study. Women who also had antenatal corticosteroids during the index pregnancy were excluded from the study. Also, women that carried their pregnancy beyond 36 weeks 7 days (term) and those that had intrauterine foetal death were excluded from the analysis.

Gestational age was calculated from the date of the last menstrual period or early scan (before 20 weeks of gestation).

The study was conducted between February 2018 and May 2019 at the Department of Obstetrics and Gynecology and the Department of Paediatrics Ahmadu Bello University Teaching Hospital, Shika, Nigeria. Recruitment was stopped when the desired sample size was achieved.
Intervention

The first study group received 2 doses of 12mg intramuscular dexamethasone sodium phosphate given 12 hours apart. (Produced by Taizhou Overseas International Ltd. 126-128 Qingnian Road Jiaojiang, Taizhou, Zhejiang, China). This was available as an already constituted clear liquid form. A total of 3ml was given per dose.

The second study group received 2 doses of 12mg of intramuscular betamethasone sodium phosphate given 12 hours apart (USP 12601, CAT No 1068004, Lot: R004E0, Twin brook Pkwy, Rockville MD, +1-301-881-0666). This was available in powder form and constituted in batches. The constituted drug appears in a clear liquid form. A total of 3ml was given per dose. The constituted drug was stored for a maximum of 120 days in the refrigerator according to the manufacturer's instructions.

The control group received 2 doses of intramuscular water for injection as a placebo given 12 hours apart (Produced by Juhel Pharmaceutical Limited, Nigeria). A total of 3ml was given per dose.

All drugs were constituted and dispensed by a research assistant from the research unit of the pharmacy department of Ahmadu Bello University Teaching Hospital in sterile syringes for immediate administration. All drugs were the same in appearance and volume.

Any woman who has had at least one dose of the intervention is considered to have had an intervention.

Outcome measures
Primary outcome measure:
Respiratory Distress:

(a) Tachypnoea with grunting, recession, or nasal flaring with diffuse reticulogranular infiltrate on X-ray.
(b) Respiratory distress requiring the need for respiratory support by 72 hours of age and will consist of one or more of the following:

Requirement for intranasal oxygen for ≥ 4 hours
Requirement for Bubble Continuous Positive Airway Pressure.

Secondary outcome measures:
1. Transient tachypnoea of the newborn: Respiratory distress resolved within 72 hours of life without diffuse reticulogranular infiltrate.
2. Admission into Special Care Baby Unit (SCBU)/Neonatal Intensive Care Unit (NICU):
Stay in the SCBU/NICU for more than 12 hours within the first 72 hours of life excluding admission after discharge. The period of observation is not considered as admission. (All preterm neonates are routinely taken to the SCBU for observation immediately after delivery.)
3. Apnoea: an unexplained episode of cessation of breathing for 20 seconds or longer, or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, and/or marked hypotonia.
4. Need for resuscitation at birth: Failure of the newborn to cry and/or initiate spontaneous breathing at birth. To be determined by skilled birth attendants who conduct the delivery.

5. Neonatal hypoglycaemia: Blood glucose level less than 2.2mmol/L at 3 hours after delivery.
6. Neonatal sepsis: Hypothermia or pyrexia and clinical evidence of sepsis in any organ/system.
7. Neonatal death.
8. Maternal sepsis: Clinical evidence of endometritis characterized by pyrexia ≥ 38.0 sub-involution of the uterus and foul-smelling lochia.

Sample size

The sample size for each group was determined by using the statistical formula for comparison of proportions as follows:

$n = 1/((1-f)) \times (2\times〖(Z_\alpha+Z_\beta)〗^2\times P\times(1-P))/〖(P0-P1)^2$

Where n = minimum sample size

P0= the proportion of participants in the control group that was expected to develop any morbidity. A study by Porto et al in Brazil reported that up to 23% (0.23) of late preterm neonates developed some form of respiratory morbidity. Thus, this was used for the calculation of the sample size for this study.

P1 = the proportion of participants in the experimental group that was expected to exhibit the outcome of interest which is respiratory morbidity. For the purpose of this study, a reduction to 10% (0.10) was considered clinically significant in this study.

Zα = was determined from a statistical table based on the value of the level of significance. For this study, it was set at 0.05. Therefore, Zα= 1.96.

Zβ = was determined from a statistical table based on the acceptable power of comparison between the 2 groups. For this study, a power of 80% (0.80) was used, therefore Zβ= 0.84.
f = was the proportion of study participants who are expected to be lost to follow up. For this study f = 10% (0.1)
n = 49.1
Each group was rounded up to 50.

Randomization

The WINPEPI ^{R} version 11.65 software was used to generate the table of random numbers.
The table of random numbers was developed and kept with the research unit of the pharmacy department, Ahmadu Bello University Teaching Hospital, where the study drugs were kept and dispensed for use once patients were recruited for the study. The randomization code was only made available to the principal investigator after the completion of the trial for data analysis.

Patients who fulfilled the inclusion criteria were enrolled by the team on call or managing team as they presented to the hospital. After obtaining written consent, the participants were requested to pick one of the brown envelopes that contained the randomization number. A proforma was then filled out for the participants indicating the randomization number. The randomization number was taken to the pharmacy unit by the attending staff where the drugs were dispensed for administration to the participants.

Blinding

All drugs were constituted and dispensed by a research assistant from the research unit of the pharmacy department of Ahmadu Bello University Teaching Hospital in sterile syringes for immediate administration. All drugs were exactly the same in appearance and volume which was 3ml. Each drug was given as 6ml of clear fluid. The principal investigator, research assistants, and special care baby unit/neonatal intensive care unit staff were not aware of the group the women and neonates belonged to because all drugs appeared exactly the same at the point of administration.

Statistical methods

The data obtained was analyzed using SPSS version 23.0. A pairwise analysis [9] was done to determine where the differences exist between the groups. Pairwise analysis (betamethasone vs. placebo, dexamethasone vs. placebo, betamethasone vs. dexamethasone) was done for statistical analysis. The socio-demographic characteristics, reproductive profile, and perinatal characteristics of the women and their neonates in the group were compared with student t-test for continuous variables, Pearson's Chi-Square (χ^2) test, and Fisher's test for discrete variables with normal distribution and Mann-Whitney U test for continuous variables or those with non-normal distribution. P values for all tests were two-tailed and the level of significance was defined at 1%. Relative risk with confidence interval was used to determine the effects of corticosteroid treatment on perinatal and maternal outcomes. Maternal and perinatal characteristics of the participants that were statistically significant between the groups were subjected to logistic regression to determine their effect on the statistically significant outcome measures.

Funding

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However, the funding body did not participate in the design, implementation, and write-up of the study.

Ethical approval

Ethical approval to conduct the study was sought from the Health Research and Ethics Committee of Ahmadu Bello University Teaching Hospital Shika. The application was reviewed by the committee and permission to conduct the study was given on 07/08/2017 with reference number ABUTHZ/HREC/Y3/2017 (NHREC/10/12/2015; D-U-N-S-No 954524802; ABUTH/HREC/CL/05/).

Results

Recruitment

During the period of study, a total of 150 pregnant women were randomized for the study. Out of these women, 5 women carried their pregnancies to term, 4 withdrew consent, 2 were discharged home and subsequently lost to follow up and 1 had intrauterine fetal death. The remaining 138 pregnant women were included in the study. Among these women, there were 6 sets of twins and a set of triplets. This gave a total number of 146 neonates in the study. Of these neonates, 48 were exposed to antenatal placebo, 49 were exposed to antenatal betamethasone and 49 were exposed to antenatal dexamethasone. (Figure 1.)

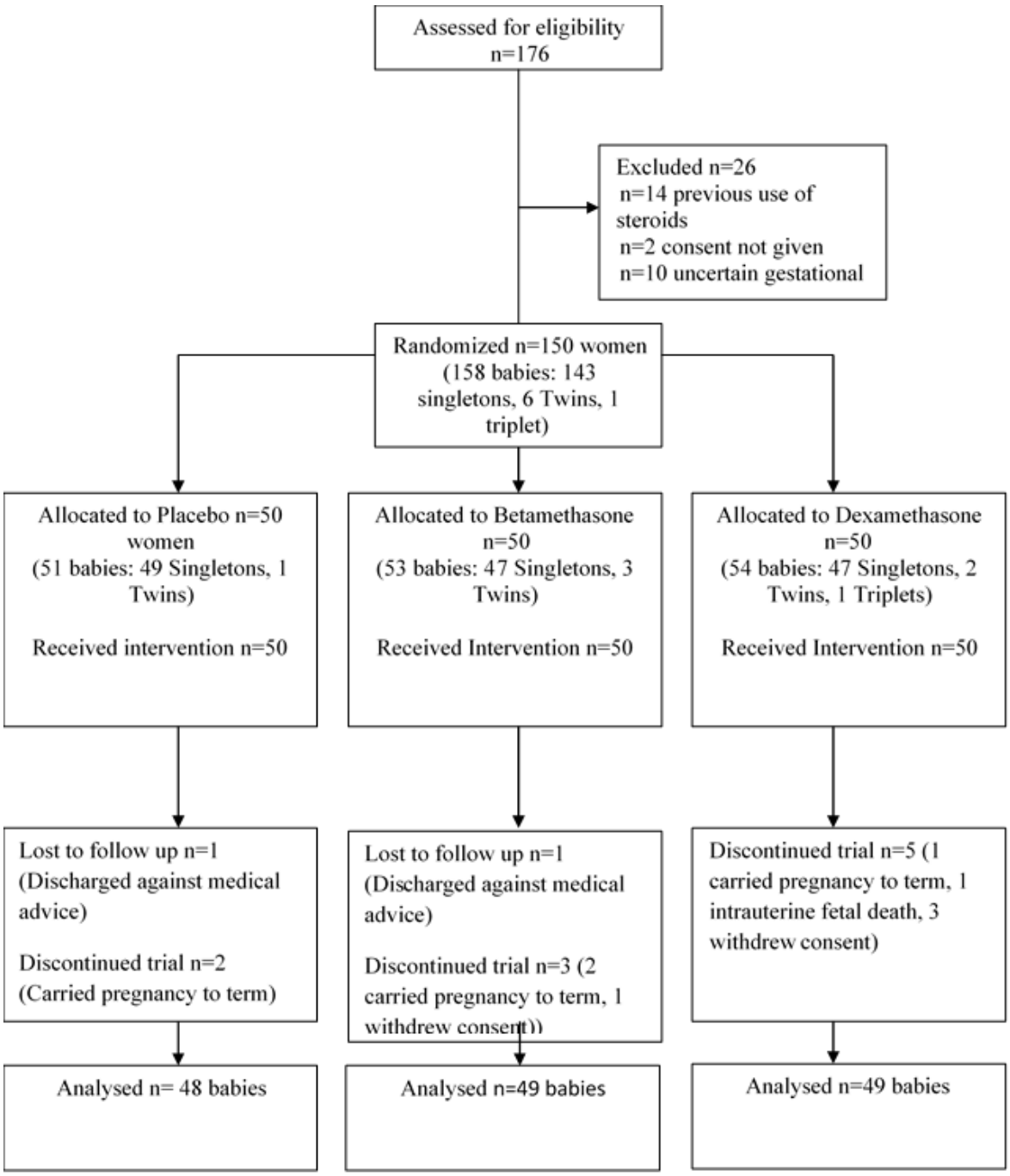

Figure 1: Screening, Enrollment, Randomization and Follow-up

The baseline characteristics of the participants were similar across all groups. (Tables 1 and 2) All group analyses showed a statistically significant difference in both 1-minute and 5-minute APGAR. (Table 2) The betamethasone group had higher 1minute and 5-minute APGAR when compared to the control group and the difference was statistically significant (p= 0.011) for 1-minute APGAR but not significantly different for the 5-minute APGAR (p= 0.041) when pairwise analysis was done. Also, the dexamethasone group had higher 1-minute and 5-minute APGAR when compared to the control group but pairwise analysis showed that the difference was not statistically significant (p=0.166; p=0.499 respectively). There was also no significant difference in the 1-minute and 5-minute APGAR between the betamethasone and dexamethasone groups (p=0.296; p=0.255 respectively) following a pairwise analysis. Other characteristics did not differ significantly between the groups. (Tables 1 and 2)

Table 1: Baseline Characteristics of Participants

Maternal Profile	Frequency (%)			p-value
	Control (n=48)	**Betamethasone (n=49)**	**Dexamethasone (n=49)**	
Socio-Demographic Characteristics				
Mean age (years)	*28.4 ± 5.9*	*28.1 ± 6.3*	*27.7 ± 7.4*	*0.935*
Tribe				
Hausa	*32 (66.7)*	*27 (55.1)*	*35 (71.4)*	*0.614*
Non-Hausa	*16 (33.3)*	*22 (44.9)*	*14 (28.6)*	
Level of Education				
Informal	*3(6.2)*	*3 (6.1)*	*10 (20.4)*	*0.129*
Primary	*15 (31.2)*	*21 (42.9)*	*17 (34.7)*	
Secondary	*22 (45.8)*	*16 (32.7)*	*14 (28.6)*	
Tertiary	*8 (16.7)*	*9 (18.4)*	*8 (16.3)*	
Reproductive Characteristics				
Median Parity IQR	1.5(0-3)	2.0(1-3)	2.0(1.3)	0.369
Gestational Age at Delivery				
34weeks - 34weeks 6days	*7 (14.6)*	*6 (12.2)*	*9 (18.4)*	*0.131*
35weeks - 35weeks 6days	*10(20.8)*	*14 (28.6)*	*9(18.4)*	
36weeks - 36weeks 6days	*21 (43.8)*	*20(40.8)*	*23(46.9)*	
37weeks - 37weeks 6days	*10 (20.8)*	*9 (18.4)*	*8(16.3)*	
Indication for Trial Entry				
Pre-eclampsia/eclampsia	*17 (35.4)*	*18 (36.7)*	*20 (40.8)*	*0.776*
Gestational/chronic hypertension	*2 (4.2)*	*5 (10.2)*	*5 (10.2)*	
Pre-term labour with intact membrane	*18 (37.5)*	*15 (30.6)*	*12 (24.5)*	
Ruptured membrane	*7 (14.6)*	*6 (12.2)*	*6 (12.2)*	
*Others**	*4 (8.3)*	*5 (10.2)*	*6 (12.2)*	

*Others: Hypocalcemia in Pregnancy, Colorectal Cancer in pregnancy, Vaso-occlusive crises in pregnancy, Suspected Macrosomia.

Table 2. Perinatal Characteristics

Perinatal Characteristics	Frequency (percentage) **Control (n=48)**	**Betamethasone (n=49)**	**Dexamethasone (n=49)**	**p-value**
Mode of Delivery				
Vaginal delivery	*16 (33.3)*	*26 (53.1)*	*16 (32.7)*	*0.069*
Caesarean section	*32 (66.7)*	*23 (46.9)*	*33 (67.3)*	
Dose received				
Complete dose	*33(68.8)*	*30(61.2)*	*34(69.4)*	*0.414*
Incomplete dose	*15(31.2)*	*19(38.8)*	*15(30.6)*	
Neonatal Characteristics				
Sex				
Male	*23 (47.9)*	*20 (40.8)*	*21 (42.9)*	*0.779*
Female	*25 (52.1)*	*29 (59.2)*	*28 (57.1)*	
Mean Birth Weight	2.5 ± 0.4	2.5 ± 0.4	2.3 ± 0.4	0.630
Mean APGAR at 1 min.	7.0 ± 2.0	7.8 ± 0.8	7.5 ± 1.7	0.001
Mean APGAR at 5 mins.	8.4 ± 1.5	9.0 ± 0.9	8.6 ± 1.6	0.001

The need for neonatal resuscitation was significantly higher (RR: 7.0; CI: 2.49-19.4; p = <0.001) in the placebo group when compared to the betamethasone group. (Table 3) and also significantly higher (RR:4.0; CI: 1.86-26.03; p= 0.01) in the placebo group when compared to the dexamethasone group. (Table 3). There was no significant difference in both primary outcome measures and other secondary outcome measures between the Betamethasone vs. placebo and the Dexamethasone vs. placebo groups (Tables 3).

Table 3: Outcome measures with Betamethasone vs placebo and Dexamethasone vs placebo

Outcome measure	**Betamethasone n=49**	**Placebo n=48**	**RR(CI)**	**p-value**	**Dexamethasone n=49**	**Placebo n=48**	**RR(CI)**	**p-value**
Primary outcome								
Respiratory Distress Syndrome	*0(0)*	*1(2.1)*	*-**	*-**	*1(2.0)*	*1(2.1)*	*1.0(0.06-16.89)*	*0.98*
Secondary outcome								
Need for neonatal resuscitation	*3(6.1)*	*15(31.2)*	*7.0(2.49-19.46)*	*<0.001†*	*5(10.2)*	*15(31.3)*	*4.0(1.86-26.03)*	*0.01†*
Transient tachypnoea	*0(0)*	*1(2.1)*	*0.5(0.05-4.60)*	*0.05*	*0(0)*	*1(2.1)*	*-**	*-**
Apnoea	*0(0)*	*0(0)*	*-**	*-**	*0(0)*	*0(0)*	*-**	*-**
Neonatal Hypoglycaemia	*4(8.2)*	*2(4.2)*	*0.5(0.10-2.40)*	*0.36*	*7(14.3)*	*2(4.2)*	*0.5(0.09-2.81)*	*0.42*
Special Care Baby Unit admission	*4(8.2)*	*6(12.5)*	*1.6(0.52-4.93)*	*0.40*	*2(4.1)*	*6(12.5)*	*1.6(0.42-6.10)*	*0.48*
Neonatal sepsis	*0(0)*	*1(2.1)*	*-**	*-**	*2(4.1)*	*1(2.1)*	*1.0(0.94-1.02)*	*0.31*
Neonatal death	*0(0)*	*0(0)*	*-**	*-**	*0(0)*	*0(0)*	*-**	*-**
Maternal sepsis	*2(4.1)*	*1(2.1)*	*0.5(0.05-4.60)*	*0.53*	*2(4.1)*	*1(2.1)*	*0.5(0.04-5.70)*	*0.57*

RR Relative risk, CI Confidence interval, *Not estimated, † statistically significant

No significant differences were found between the Betamethasone Vs the Dexamethasone groups in both primary and secondary outcome measures. (Table 4).

Table 4: Outcome measures with Betamethasone vs Dexamethasone

Outcome measure	Betamethasone n=49	Dexamethasone n=49	Relative risk	Confidence interval	p-value
Primary outcome					
Respiratory Distress Syndrome	*0(0)*	*1(2.0)*	-	-	-
Secondary outcome					
Need for neonatal resuscitation	*3(6.1)*	*5(44)*	*0.5*	*0.21-1.50*	*0.18*
Transient tachypnoea	*0(0)*	*0(0)*	-	-	-*
Apnoea	*0(0)*	*0(0)*	-	-	-*
Neonatal hypoglycaemia	*4(8.2)*	*7(14.3)*	*0.5*	*0.22-1.23*	*0.09*
Special Care Baby Unit admission	*4(8.2)*	*2(4.1)*	*2.0*	*0.68-6.09*	*0.15*
Neonatal sepsis	*0(0)*	*2(4.1)*	*1.7*	*1.53-1.90*	*0.43*
Neonatal death	*0(0)*	*0(0)*	-	-	-*
Maternal sepsis	*2(4.1)*	*2(4.1)*	*1.0*	*0.27-3.56*	*0.62*

*not estimated

A logistic regression analysis was done to determine the relationship between the need for resuscitation at birth and the study group of the women while adjusting for a 1-minute APGAR score that was significantly higher in the betamethasone group when compared to the placebo group. The result showed that after adjusting for 1-minute APGAR score there was a significant reduction in the likelihood of need for neonatal resuscitation by about 85% (ExpB=0.157, p=0.005) when betamethasone was used compared to placebo.

Discussion

The incidence of respiratory distress syndrome among late preterm neonates was low in our study. The incidence of respiratory distress varies with race. [4] A low incidence of respiratory distress syndrome has been reported among blacks. [4] and may explain the low incidence of respiratory distress in our study coupled with the fact that compared to other categories of preterm births, its incidence is lower in late preterm neonates. There was no significant difference in the incidence of respiratory distress syndrome between the group exposed to placebo versus antenatal betamethasone (p= 0.98, RR 1.0, CI 0.09-11.55), the group exposed to placebo versus antenatal dexamethasone (p=0.98, RR=1.0, CI 0.06-16.87) and the group exposed to antenatal betamethasone versus antenatal dexamethasone (p=0.31, RR=0.5, CI 0.09-2.42). This is similar to the findings of Porto et al [10] who reported a low incidence of respiratory distress among late preterm neonates exposed to antenatal betamethasone and those exposed to placebo (1.4% and 0.8% respectively) with no significant difference in the incidence of respiratory distress between the 2 groups (p=0.54, RR 1.90). However, this is not consistent with the findings of Balci et al [11] who reported an incidence of 16% among late preterm neonates who did not receive antenatal steroids and an incidence of 4% among those who received betamethasone and the difference between the two groups was statistically significant (p=0.046, OR 0.21). The study by Balci et al [11] found a significant difference in the incidence of respiratory distress in their study possibly due to the open-label trial method, which may have introduced some bias unlike our study and that by Porto et al [10] which were both randomized

double-blinded. A similar double-blind randomized controlled trial by Gyamfi-Bannerman et al [12] found a statistically significant higher incidence of the primary outcome in the late preterm neonates in the control group, the primary outcome was a neonatal composite of treatment including the use of CPAP or high flow nasal cannula at least for 2 hours, supplemental oxygen with a fraction of inspired oxygen of at least 0.30 for at least 4 hours, extracorporeal membrane oxygen, or mechanical ventilation or stillbirth or neonatal death rather than respiratory distress alone. This may account for the difference in findings.

The incidence of transient tachypnoea in the newborn was also low in this study with only one neonate (2.1%) in the group exposed to placebo developing the outcome (Tables 3). Our finding of the low incidence of transient tachypnoea was not consistent with a report by Gyamfi-Bannerman et al[12] who reported an incidence of transient tachypnoea of the newborn among late preterm neonates exposed to antenatal betamethasone as 6.7% and 9.9% in those exposed placebo (9.9%) (p=0.002, RR 0.68 CI 0.53-0.87). A higher incidence was reported by Porto et al [10] where 24% of late preterm neonates exposed to antenatal betamethasone and 22% of those exposed to placebo developed transient tachypnoea. However, there was no significant difference between the groups. The low incidence of transient tachypnoea of the newborn in our study is in keeping with the low incidence of respiratory distress syndrome noted in the study.
This study showed a statistically significant reduction in the need for neonatal resuscitation at birth among the neonates exposed to antenatal betamethasone compared to those exposed to placebo (p <0.001, RR 7.0, CI 2.49-19.46) and also the neonates exposed to antenatal dexamethasone compared to those exposed to placebo (p=0.010, RR 4.0, CI 1.86-26.03). This means that neonates born to women who received a placebo were 7 times more likely to need neonatal resuscitation at birth compared to neonates born to women who received betamethasone and 4 times more likely to need resuscitation at birth compared to neonates born to women who received dexamethasone. The use of betamethasone was associated with a 40% decrease in need for resuscitation at birth compared to the use of dexamethasone though this was not statistically significant (p=0.461).

Other studies have also reported a decrease in the need for neonatal resuscitation at birth in women exposed to antenatal corticosteroids when compared with women exposed to placebo. [11, 12]. This finding is of significance especially in our environment so that women seen during the late preterm period with the probability of having a late preterm delivery can be offered antenatal steroids because such deliveries may occur in the absence of skilled birth attendants that can adequately offer neonatal resuscitation at birth.

The need for admission into SCBU was highest among the placebo group. However, the differences observed were not statistically significant (Tables 3, 4).

Apnoea was not reported in any of the study or control groups. This may be because clinical monitoring was used to detect apnoea rather than a continuous electronic recording of the vital signs of the neonates. This has been observed in other studies where a lack of correlation between nurses' records with continuous electronically recorded events has been demonstrated. [13, 14]. In a randomized controlled trial on the use of betamethasone for women at risk for late preterm delivery, apnoea was reported to occur in 2.3% of the group that had betamethasone and in 2.6% of the control group with no significant difference between the two groups (p=0.57). [12] Other studies on the use of antenatal corticosteroids in late preterm neonates did not report on apnoea. [10, 11]

The differences in the incidences of hypoglycemia between the groups were not statistically significant (Table 3,4). Conflicting reports exist in the literature with regard to the incidence of hypoglycemia in neonates following exposure to antenatal corticosteroids. While some authors [5, 12] reported an increase in the rate of hypoglycemia among infants exposed to antenatal corticosteroids, others did not [6]. A systematic review and meta-analysis of randomized controlled trials on the use of antenatal

corticosteroids in the near term and term foetuses also showed an increased risk of neonatal hypoglycemia in neonates whose mothers received antenatal corticosteroids at more than 34 weeks gestation. [5] However, no adverse effects were reported in all the trials. This inconsistency may be due to the fact that neonatal hypoglycemia is a common late preterm neonatal complication irrespective of the use of antenatal corticosteroids within the period. [15] Incidence of neonatal and maternal sepsis were low and the differences between the groups were not statistically significant. (Tables 3, 4). This is consistent with existing literature. [12]

Conclusion

This study found that the use of antenatal corticosteroids in late preterm delivery significantly reduced the need for neonatal resuscitation at birth but may not have an effect on the incidence of respiratory distress syndrome and other neonatal and maternal morbidity.

In view of the findings in this study, we recommend the use of antenatal corticosteroids in women at risk of preterm delivery with the aim of reducing the need for neonatal resuscitation at birth. However, there is still the need for larger trials on the effect of the use of antenatal corticosteroids in late preterm deliveries to prevent neonatal morbidity and minimize side effects on both mother and neonates.

Strengths and limitations

The major strength of this study is the fact that it was a double-blind randomized controlled trial and both dexamethasone and betamethasone were used as antenatal corticosteroids. However, it was conducted in a single center with a small sample size which is a limitation.

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