Neonatal and maternal outcomes after betamethasone administration in the management of late-preterm premature rupture of membranes (PROM)

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Introduction

- Infants born in the late preterm period are more likely to experience respiratory issues, as well as increased morbidity and mortality compared to term infants[1].
- The ALPS randomized trial concluded that antenatal betamethasone reduced the rate of neonatal respiratory complications in pregnancies at risk for late preterm delivery, including those with PPROM, based on a subgroup analysis test for interaction.
- Previous research also suggests no increase in risk for neonatal or maternal infection with administration of antenatal steroids in the setting of PPROM, although most assessed gestational age less than 34 weeks[2].
- Clinical practice reveals that less one half of eligible patients receive antenatal betamethasone in the setting of late preterm PROM, indicating a potential underlying concern for maternal or neonatal risk and the need for further research focused on this subgroup.

Objective:

- Assess the impact of betamethasone administration in the immediate delivery management of late-preterm premature rupture of membranes (PROM) on maternal and neonatal outcomes.

Methods

- Retrospective review of singleton pregnancies with PROM delivering at 34 to 36 weeks 5 days gestation within a healthcare maintenance organization, 2017 to 2019.
- Utilized inclusion criteria and outcome measures similar to the ALPS trial.
- Treatment with one or two doses of betamethasone prior to delivery was compared with no treatment.
- The primary outcome was a neonatal composite of respiratory complications of one or more: respiratory distress syndrome, respiratory arrest, transient tachypnea, use of CPAP or HFNC. Statistical analysis utilized Chi-square and multivariate logistic regression.

References

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Betamethasone administration with immediate delivery management for **late-preterm PROM** was **not associated** with a significant **reduction in the rate of neonatal respiratory complications** in our study.

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Results

- The primary composite outcome occurred in 44 of 328 (13.4%) in the betamethasone group versus 122 of 699 (17.5%) in the control group (RR 0.77; 95% confidence interval (CI), 0.5 to 1.1; P=0.1).
- The primary outcome occurred more often following cesarean versus spontaneous vaginal delivery (OR 2.5; 95% CI, 1.7 to 3.7, p <.0001).
- The mean gestational age and median time from admission to delivery did not differ between groups, 35.4 weeks and 17.3 versus 17.6 hours (p=0.8) respectively, indicating immediate delivery management.
- The rate of chorioamnionitis was less in the betamethasone group, at 3.4% versus 6.6% in the control group, (RR 0.51; 95% CI 0.2 to 0.97, p=0.04).
- Endometritis following delivery did not differ between the groups, whereas neonatal sepsis occurred more often in the betamethasone group at 1.5 % versus 0.3%, (RR 5.3; 95% CI, 1 to 27, p=0.04).
- A higher rate of neonatal hypoglycemia was also observed in the betamethasone group (15.5% vs. 10.7%; RR 1.4, 95% CI, 1.0 to 2.0; p=0.03).

Table 1: Maternal and neonatal outcomes after delivery

Outcome	Betamethasone (N=328)	Control (N=699)	p-value†
Primary outcome:			
Composite of neonatal respiratory disorders*			0.1
0 or none	284 (86.6%)	577 (82.6%)	
1, 2 or 3 present	44(13.4%)	122(17.4%)	
Mode of delivery:			0.04
Cesarean delivery	44 (13.4%)	134 (19.1%)	
Operative vaginal delivery	10 (3.0%)	13 (1.8%)	
Spontaneous vaginal delivery	274 (83.5%)	552 (78.9%)	
Maternal secondary outcomes:			
Presence of chorioamnionitis	11 (3.4%)	46 (6.6%)	0.03
Endometritis following delivery	1 (0.3%)	6 (0.9%)	0.31
Neonatal secondary outcomes:			
NICU admission	64 (19.2%)	134 (19.5%)	0.89
Hypoglycemia	51 (15.5%)	75 (10.7%)	0.02
Hyperbilirubinemia	157 (48.0%)	314 (44.9%)	0.37
Necrotizing enterocolitis	0 (0.0%)	1 (0.1%)	0.46
Intraventricular hemorrhage	1 (0.3%)	3 (0.4%)	0.76
Hypothermia	4 (2.1%)	15 (1.2%)	0.30
Sepsis	5 (1.5%)	2 (0.3%)	0.02

*Composite of neonatal respiratory disorders include having one or more of the following: respiratory distress syndrome, respiratory arrest of the newborn, transient tachypnea of the newborn, and the use of CPAP or HFNC. Data are n (%); †p-value from Chi-square

Table 2: Adjusted odds ratios of composite of neonatal respiratory disorders (1+ vs 0)

Variable	Adjusted odds ratio† [95% confidence interval]	p-value
Betamethasone vs. Control	0.78 [0.53-1.16]	0.23
Cesarean delivery vs. Spontaneous vaginal delivery	2.5 [1.7-3.7]	<0.0001
Operative vaginal delivery vs. Spontaneous vaginal delivery	1.1 [0.3-3.9]	0.8

†Multivariate logistic regression analysis was performed adjusting for maternal and neonatal characteristics.

Discussion

- Betamethasone for late-preterm PROM was not associated with a statistically significant reduction in the rate of neonatal respiratory complications, which contrasts with the ALPS trial.
- Maternal infectious morbidity was not increased, although we observed higher rates of neonatal sepsis, and this concern has previously been raised by the 2016 Antenatal Corticosteroids (ACT) trial, particularly for newborns with birthweight >25%[3].
- A higher incidence of neonatal hypoglycemia following antenatal betamethasone exposure in the late-preterm period has previously been reported in a systemic review and meta-analysis of randomized control trials in similar populations[4].
- Our study reaffirms that cesarean delivery remains a significant risk factor for neonatal respiratory morbidity in the late preterm, regardless of steroid administration.