Time interval from late preterm antenatal corticosteroid administration to delivery and the impact on neonatal outcomes

Moti Gulersen[1], Cynthia Gyamfi-Bannerman[2], Michelle Greenman[1], Erez Lenchner[3], Burton Rochelson[1], Eran Bornstein[4]

[1]Department of Obstetrics and Gynecology, North Shore University Hospital – Zucker School of Medicine at Hofstra/Northwell, Manhasset, [2]Department of Obstetrics and Gynecology, Columbia University Irving Medical Center, New York, NY, [3]Biostatistics and Data Management, New York University Rory Meyers College of Nursing, New York, NY, [4]Department of Obstetrics and Gynecology, Lenox Hill Hospital – Zucker School of Medicine at Hofstra/Northwell, New York, NY

DONALD AND BARBARA ZUCKER SCHOOL of MEDICINE AT HOFSTRA/NORTHWELL

COLUMBIA

Abstract

Objective: While administration of antenatal corticosteroids (ACS) has been shown to decrease neonatal respiratory morbidity when given to women at risk for late preterm birth, the time interval from ACS to delivery associated with the greatest neonatal benefit remains unknown. Therefore, we set out to evaluate the association between time interval from administration of late preterm ACS to delivery and several adverse neonatal outcomes.
Methods: Retrospective cohort of all singleton newborns who were exposed to one or two doses of an ACS course in the late preterm period (34 0/7-36 6/7 weeks) within a large health system between November 2017 and March 2020. Newborns exposed to ACS prior to 34 weeks, major fetal structural malformations and chromosomal disorders were excluded. Cases were stratified based on the time interval from ACS administration to delivery: < 2, 2-7, and > 7 days. The rates of several adverse neonatal outcomes (i.e. transient tachypnea of the newborn [TTN], respiratory distress syndrome [RDS], and hypoglycemia) were compared among the three groups. Multivariable logistic regression was performed to evaluate the association of time interval with neonatal outcomes, while adjusting for potential confounders. Data were presented as adjusted Odds Ratios (aOR) with 95% confidence intervals (95% CI), and statistical significance was defined as $P < 0.05$.
Results: 1,248 newborns comprised the study cohort. There were statistically significant differences in maternal characteristics such as nulliparity, pregnancies complicated by hypertensive disorders and fetal growth restriction, gestational age at ACS administration, gestational age at delivery and mode of delivery among the three groups. There was a significantly increased risk of TTN associated with delivery < 2 days (aOR 3.80, 95% CI 1.42-10.18) and > 7 days (aOR 3.39, 95% CI 1.12-10.27) of ACS administration. The risk of hypoglycemia was highest in the delivery < 2 days group (aOR 3.30, 95% CI 2.01-5.41) and decreased as time interval from ACS to delivery increased (aOR 0.44, 95% CI 0.26-0.73 for delivery > 7 days). There was no statistically significant association between time interval of ACS administration to delivery and RDS.
Conclusions: Adverse neonatal outcomes such as TTN and hypoglycemia are more common when late preterm birth occurs < 2 days after ACS administration. Moreover, late preterm birth > 7 days after ACS administration is associated with an increased risk of TTN, but a decreased risk of hypoglycemia. Understanding the impact of ACS timing on neonatal outcomes is essential in caring for patients at risk for late preterm birth.

Objectives

To determine if there is an association between time interval from late preterm ACS administration to delivery and adverse neonatal outcomes

Study Design

- Retrospective cohort of all newborns from singleton pregnancies that were exposed to ACS in the late preterm period (34 0/7-36 6/7 weeks) within a large health system between November 2017 and March 2020
- Inclusion criteria = exposed to at least one of the two doses
- Exclusion criteria = exposed to ACS prior to late preterm period in the same pregnancy, major fetal structural malformations, confirmed chromosomal disorders
- Cases stratified based on time interval from ACS administration to delivery: < 2, 2-7, and > 7 days
  - **Neonatal outcomes compared among 3 groups = TTN, RDS, hypoglycemia**
- Statistical analysis for comparisons = Chi-squared and Wilcoxon rank-sum tests, multivariate logistic regression while adjusting for potential confounders

Results

Table 1. Comparison of baseline characteristics among study groups

	Delivered < 2 days after ACS (n=772)	Delivered 2-7 days after ACS (n=168)	Delivered >7 days after ACS (n=308)	*P* value
Maternal age (years) – mean ± SD	32.8 ± 0.19	33.4 ± 0.43	33 ± 0.29	0.34
BMI (kg/m^2) – mean ± SD	30.8 ± 0.22	31.2 ± 0.52	30.7 ± 0.34	0.71
Race or ethnic group – n (%)				
Non-Hispanic White	278 (36)	61 (36.3)	143 (46.4)	0.11
Non-Hispanic Black	140 (18.1)	35 (20.8)	46 (14.9)	
Hispanic	92 (11.9)	22 (13.1)	40 (13)	
Asian	135 (17.5)	27 (16.1)	46 (14.9)	
Other	81 (10.5)	13 (7.7)	22 (7.1)	
Unknown	46 (6)	10 (6)	11 (3.6)	
Nulliparity – n (%)	389 (50.4)	94 (56)	128 (41.6)	**0.005**
Hypertensive disorder of pregnancy – n (%)	171 (22.2)	66 (39.3)	79 (25.6)	**<0.001**
Fetal growth restriction – n (%)	34 (4.4)	18 (10.7)	22 (7.1)	**0.004**
Gestational diabetes – n (%)	73 (9.5)	17 (10.1)	25 (8.1)	0.72
Gestational age at ACS administration (weeks) – mean ± SD	35.6 ± 0.03	35.6 ± 0.06	35.1 ± 0.04	**<0.001**
Gestational age at delivery (weeks) – mean ± SD	35.7 ± 0.03	36.2 ± 0.06	38 ± 0.07	**<0.001**
Vaginal delivery – n (%)	460 (59.6)	76 (45.2)	201 (65.3)	**<0.001**

Table 2. Association of time interval from ACS administration with adverse neonatal outcomes

	Rate	Adjusted OR (95% CI)	*P* value
Transient tachypnea of the newborn			
<2 days after ACS	97/772 (12.6%)	3.80 (1.42-10.18)	**0.008**
2-7 days after ACS	6/168 (3.6%)	Reference	---
>7 days after ACS	10/308 (3.2%)	3.39 (1.12-10.27)	**0.03**
Respiratory distress syndrome			
<2 days after ACS	74/772 (9.6%)	7.44 (0.87-63.49)	0.07
2-7 days after ACS	1/168 (0.6%)	Reference	---
>7 days after ACS	2/308 (0.6%)	4.22 (0.36-49.11)	0.3
Hypoglycemia			
<2 days after ACS	383/772 (49.6%)	3.3 (2.01-5.41)	**<0.001**
2-7 days after ACS	61/168 (36.3%)	Reference	---
>7 days after ACS	47/308 (15.3%)	0.44 (0.26-0.73)	**0.001**

Odds ratios were adjusted for nulliparity, hypertensive disorders of pregnancy, fetal growth restriction, gestational diabetes, number of ACS doses (1 or 2), gestational age at delivery (as continuous variable) and mode of delivery

Conclusions

- Adverse neonatal outcomes such as TTN and hypoglycemia are more likely when late PTB occurs <2 days after ACS administration
- Late PTB >7 days after ACS administration is associated with an increased risk of TTN, but a decreased risk of hypoglycemia