OBSTETRICS

The timing of administration of antenatal corticosteroids in women with indicated preterm birth

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OBJECTIVE: We sought to determine the timing of administration of antenatal corticosteroids (AS) for indicated preterm births and to identify which indications are associated with the most optimal timing of administration.

STUDY DESIGN: This was a retrospective cohort of patients who received AS in anticipation of indicated preterm birth from 2009 through 2012 at Winthrop University Hospital, Mineola, NY. Medical records of patients who received AS, as identified through the hospital pharmacy database, were reviewed. Patients were included if they had a singleton or twin gestation and they received AS for maternal or fetal indications. Women were excluded if they received AS for spontaneous preterm labor or preterm rupture of membranes. Maternal demographic and obstetrical characteristics were compared between those who received AS $\leq$7 days vs >7 days from delivery using parametric and nonparametric tests with relative risks and 95% confidence intervals. $P < .05$ was considered significant.

RESULTS: In all, 193 patients were included in this study. Median latency from AS administration to delivery was 9 days (range, 0—83); 93 patients (48%) received AS within 7 days of delivery. There were no significant differences between the 2 groups with regards to baseline maternal characteristics. Those delivering within 7 days of AS administration were more likely to have maternal vs fetal indications (84% vs 16%).

CONCLUSION: Only 48% of patients with an indication for preterm birth received AS within 7 days of its administration. AS appear to be more optimally timed in the presence of maternal rather than fetal indications.

Key words: antenatal corticosteroids, decision to administer antenatal corticosteroids, indicated preterm birth, preterm birth, timing of antenatal corticosteroids

Cite this article as: Adams TM, Kinzler WL, Chavez MR, et al. The timing of administration of antenatal corticosteroids in women with indicated preterm birth. Am J Obstet Gynecol 2015;212:645.e1-4.

Preterm delivery occurs in 11.7% of all pregnancies in the United States and is a leading cause for perinatal morbidity and mortality.[1] Approximately one third of all preterm births are medically indicated.[2-4] Antenatal corticosteroids (AS) given to pregnant women at risk for preterm delivery <34 weeks have been long established to decrease neonatal mortality and infant morbidity including decreased frequency of respiratory distress syndrome and intraventricular hemorrhage.[5-9] Liggins and Howie[5] were the first to describe how the use of AS within 7 days of delivery leads to improved respiratory outcomes in infants who delivered between 28-34 weeks of gestation. Many studies since then have confirmed those findings.[6-9] Decreased neonatal benefits are observed if birth is >7 days from AS administration.[10-13]

Since many patients remain undelivered after AS administration, weekly AS administration will ensure delivery within a week. However, several studies have suggested that multiple weekly AS administration is associated with decreased birthweight, decreased head circumference, and increased risk of fetal adrenal suppression.[14-18] As a result, repeat dosing is not recommended by American Congress of Obstetricians and Gynecologists with the exception of a single rescue course.[19] Since it is axiomatic to do no harm, correct timing of AS administration in women at risk for preterm birth is of paramount importance.

Since more than half of the preterm births are spontaneous, we as well as other investigators have previously focused in the timing of AS steroids in the setting of threatened preterm labor with or without premature rupture of the membranes. Unfortunately, it was found that only 20-40% of women who are given AS for threatened spontaneous preterm delivery actually go on to deliver within 7 days.[20,21]

Indicated preterm birth is a significant contributor encompassing up to 40% of all preterm births based on US population statistics.[4] Yet, the data regarding timing of AS administration in indicated preterm birth are scarce.[20] Therefore, we undertook this retrospective study to determine the timing of AS administration in indicated preterm births and to identify the indications associated with the most optimal timing. We hypothesized that

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Received Aug. 20, 2014; revised Oct. 23, 2014; accepted Nov. 18, 2014.

The authors report no conflict of interest.

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0002-9378/$36.00
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http://dx.doi.org/10.1016/j.ajog.2014.11.021

indicated preterm births have an increased frequency of AS administered within 7 days of delivery and optimal administration may depend on the indication for deliver (maternal vs fetal).

Materials and Methods

This was a retrospective cohort of patients who received AS in anticipation of indicated preterm birth from 2009 through 2012 at Winthrop University Hospital, Mineola, NY. Patients who received AS were identified through the hospital pharmacy database; their medical records were then reviewed to abstract the clinical data. This study was approved by the institutional review board. The primary outcome was to determine the proportion of patients receiving AS for suspected indicated preterm birth delivering within 7 days. The secondary outcome was to determine which indications for AS administration were more frequently associated with optimal timing of AS administration. Patients were included if they had a singleton or twin gestation and they received AS between 24-34 weeks' gestation for maternal or fetal indications. Maternal indications included: preeclampsia, bleeding previa, or other maternal illness such as thrombotic thrombocytopenia purpura, acute abdomen, and supraventricular tachycardia. Fetal indications included idiopathic intrauterine growth restriction (IUGR) (without preeclampsia), abnormal fetal Doppler, oligohydramnios, nonreassuring fetal status, or placental anomaly (including vasa previa and placental hemangioma). Exclusion criteria were patients with high-order multiples, those who received AS for a threatened spontaneous preterm delivery, and incomplete records (patients who either transferred from or delivered at an outside institution). Patients who received AS for suspected abruption who had vaginal bleeding and contractions were excluded from this review, as it is unclear whether this was due to spontaneous preterm labor or abruptio placentae. Our institution's practice is to administer AS to women between 24-34 weeks' gestation who are at risk for preterm delivery. A single rescue course is considered if the first dose of AS was given >14 days prior, and the current gestational age is <34 weeks. In the setting of IUGR and oligohydramnios the decision to deliver is based on a nonreassuring fetal status as indicated by heart rate tracing or fetal biophysical profile. The decision to administer AS for a suspected indicated preterm delivery was left to the discretion of the primary provider, although all patients did receive maternal-fetal medicine consultation, who ultimately decided upon the timing of AS administration.

The latency between administration of AS and delivery was defined as the number of days between the first dose and delivery. The patients were then categorized into 1 of 2 groups: optimal timing (those with a latency of ≤7 days) and suboptimal timing (those with a latency of >7 days). Patients who received a rescue course were analyzed in the suboptimal group. Variables reviewed included maternal age, race, gravidity/parity, gestational age at time of AS administration, number of doses of AS given, gestational age at delivery, history of preterm delivery, prior cesarean delivery, history of chronic hypertension, and indication for AS administration as recorded in the medical record. The optimal and suboptimal groups were then compared using the appropriate parametric and nonparametric tests. To ensure comparability with respect to the circumstances of care, between those with optimal vs suboptimal timing of AS administration, we used the comparability scoring system as proposed by Vintzileos et al.[22] We used χ^2 testing to compare categorical data, Student *t* test was used to compare continuous data, and the Wilcoxon rank sum test was used to compare ordinal data. $P < .05$ was considered significant. Relative risks and 95% confidence intervals were calculated. Multivariable regression analysis was performed to calculate adjusted relative risks.

TABLE 1
Comparison of baseline characteristics between optimal vs suboptimal timing groups

Factor	≤7 d, n = 93	>7 d, n = 100	*P* value
Age, y	31.7 (± 5.5)	31.9 (± 5.4)	.8
Race			
White	49 (53%)	59 (59%)	.2
Black	25 (27%)	21 (21%)	.2
Other	19 (20%)	20 (20%)	.5
Gravidity	2 (1–12)	2 (1–7)	.5
Prior preterm delivery	20 (22%)	12 (12%)	.04
Prior cesarean delivery	26 (28%)	22 (22%)	.2
History of chronic hypertension	17 (18%)	18 (18%)	.5
Current tobacco use	4 (4%)	6 (6%)	.3
Gestational age at time of AS	30.4 (± 2.8)	30.4 (± 2.9)	1.0
Gestational age at delivery	30.7 (± 2.7)	34.7 (± 3.0)	< .01

Data expressed as n (%), median (range), and mean (± SD).

AS, antenatal corticosteroids.

Adams. Antenatal corticosteroids timing in indicated preterm birth. Am J Obstet Gynecol 2015.

Results

A total of 1031 patients were identified through the hospital pharmacy database as having received betamethasone from 2009 through 2012. In all, 838 patients were excluded (756 received AS for spontaneous preterm labor, 76 had incomplete records, and 6 had triplet gestations), leaving 193 patients available for review. The median latency from AS to delivery was 9 days (range, 0–83); 93 patients (48%) received AS within 7 days of delivery. There were no significant differences in maternal age, race, or gravidity between the 2 groups. Women with optimal timing had an earlier gestational age at delivery than those

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