OBSTETRICS

Evaluation of strategies regarding management of imminent preterm delivery before 32 weeks of gestation: a regional cohort study among 1375 women in the Netherlands

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OBJECTIVE: To evaluate the management of imminent preterm delivery with respect to prescription of antenatal corticosteroids (ACS) and referral to a tertiary center.

STUDY DESIGN: A retrospective cohort study existing of 1 perinatal center and 9 referring hospitals. All women who received their first dose of ACS in 1 of the 10 hospitals between 24+0 and 32+0 weeks of gestation and/or delivered before 32 weeks of gestation from 2005 until 2010. Patients were identified using the electronic database of hospital pharmacies. Main outcome measures were time interval from administration to delivery for different indications and number of women who were not referred in time to a tertiary center.

RESULTS: In total, 1375 women received ACS. Main indications were suspected preterm labor (44.7%), preterm prelabor rupture of membranes (15.9%), maternal indication (12.8%), fetal indication (9.2%) and vaginal blood loss (8.4%). Overall, 467 (34.0%) women delivered ≤7 days after ACS administration; 8.7% of women with vaginal blood loss and 54.5% of women with maternal indication. Among the 931 women who received ACS in the secondary hospitals, 452 (48.5%) women were referred to a tertiary hospital and 89 (6.5%) women delivered in a secondary hospital with a gestational age of less than 32 weeks.

CONCLUSION: One-third of all women receiving ACS delivered within 7 days and half of the women who received ACS in a secondary hospital were referred to a tertiary center. There seems to be room for improvement regarding the timing of ACS administration and subsequently referral to a tertiary center.

Key words: antenatal corticosteroids, pregnancy, preterm birth, referral policy, time interval

Cite this article as: Boesveld M, Oudijk MA, Koenen SV, et al. Evaluation of strategies regarding management of imminent preterm delivery before 32 weeks of gestation: a regional cohort study among 1375 women in the Netherlands. Am J Obstet Gynecol 2015;212:348.e1-7.

Prematurity is still a major cause of morbidity and mortality. Preterm infants are at an increased risk of neonatal death, respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis. Treatment with antenatal corticosteroids (ACS) has major advantages in the outcome of preterm neonates, especially in infants born before 34 weeks of gestation.[1,2] Because of these great benefits, it is recommended that all women at risk of delivery between 24 + 0 and 34 + 0 weeks should receive a single course of ACS.[3,4] Furthermore, women at risk for preterm delivery and a gestational age between 24 + 0 and 32 + 0 weeks should be transferred to a perinatal center with a neonatal intensive care unit (NICU).[5,6]

The optimal effect of ACS is achieved within a time interval between administration and delivery of 1 to 7 days.[7-9] Because preterm birth is difficult to predict a significant number of women will receive ACS too early, too late, or not at all. As a consequence, some women are unnecessarily treated with this drug whereas others unjustly did not receive treatment with ACS. Approximately 50% of women given a first course of ACS remain pregnant and at risk for preterm birth after an interval of 7 days.[10] The safety and additional benefit of multiple ACS courses is still debated.

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Received July 2, 2014; revised July 29, 2014; accepted Oct. 7, 2014.

The authors report no conflict of interest.

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0002-9378/$36.00 • © 2015 Elsevier Inc. All rights reserved. • http://dx.doi.org/10.1016/j.ajog.2014.10.014

Although repeated courses of ACS may decrease perinatal mortality and morbidity, several studies have shown harmful neonatal effects, such as decreased length, weight, head circumference, and adverse behavior.[11-15] To ensure that every woman at risk for preterm delivery is treated adequately it is necessary to optimize the timing of the first course of ACS. Therefore, it is essential to evaluate prescribing patterns of ACS as well as the referral patterns of secondary hospitals to improve care for women at risk of preterm delivery. The aim of our study was to evaluate these issues in the referral area of the University Medical Center Utrecht (UMCU).

Materials and Methods

Setting

We performed a retrospective cohort study in the catchment area of the UMCU, a level 3 regional, referral, and university teaching hospital. The NICU of the UMCU is 1 of 10 Dutch level 3 NICU's, which cares for 13% of all neonates in need of intensive care in the Netherlands. There are 10 hospitals in the region, 7 nonuniversity teaching hospitals and 3 general hospitals, that refer pregnant women at risk for delivery before 32 weeks to the UMCU. Of these hospitals, 3 have a postintensive care/high-care facility. If a woman remains pregnant, she is referred back to her own hospital when there is no indication for admission to a level 3 hospital anymore. Nine of these 10 hospitals participated in the study. The region of Utrecht is a geographical area in the middle of the Netherlands with approximately 21,000 deliveries a year.

Population

We identified 2 groups of women. Firstly, all women receiving ACS, at least 1 dose of 12 mg of betamethasone (Celestone Chronodose; Schering-Plough, Kenilworth, NJ), between 24 + 0 and 32 + 0 weeks of gestation were included.

Patients were identified using the electronic database of the hospital pharmacies.[16] Because the aim of our study was to evaluate the prescribing patterns and referral patterns of these 10 hospitals, we included only women who received their first dose of ACS in one of these hospitals.

Secondly, all women delivering between 24 + 0 and 32 + 0 weeks of gestation who did not receive ACS were identified as well. We excluded women with an intrauterine fetal death, lethal congenital anomalies, and women who underwent a termination of pregnancy for maternal reasons in combination with a poor prognosis of the child (eg, severe early onset preeclampsia with severe: intrauterine growth restriction [IUGR]).

Data collection

Data were collected from January 2005 until December 2010. The medical charts were reviewed for maternal, pregnancy and neonatal characteristics. If information on follow-up was not available in the medical charts, a questionnaire was sent to the medical practitioner or midwife. We recorded the following characteristics: maternal age, multiple pregnancy, parity, previous preterm delivery, gestational age at administration of ACS, reason of suspected preterm birth, subsequent antenatal courses, transfer to a perinatal center, gestational age at delivery, interval from administration to delivery, mode of delivery, location of delivery, birthweight, sex, and admission to the NICU. Previous preterm delivery was defined as a delivery between a gestational age of 24 + 0 and 37 + 0 weeks. (4) A complete course of ACS was defined as 2 doses of 12 mg betamethasone. The indications for administration were categorized as: (1) suspected preterm labor with intact membranes (PTL), (2) preterm prelabor rupture of membranes (PPROM), (3) maternal indication, (4) fetal indication, (5) vaginal blood loss (VBL), (6) multiple indications. Maternal indications included: pregnancy induced hypertension, preeclampsia (PE), and HELLP-syndrome (hemolysis, elevated liver enzymes, and low platelet count). Fetal indications included: IUGR, with or without Doppler abnormalities, and suspected fetal distress (abnormalities of the cardiotocogram). VBL included: blood loss because of placenta previa or bleeding of unknown origin. The reasons for no administration of ACS were also noted and categorized as: (1) acute fetal distress, (2) poor prognosis regarding viability, (3) advanced delivery, and (4) no specific reason. It was categorized as acute fetal distress if there was an indication for an emergency cesarean delivery because of fetal reasons, including a suspicion of abruption of the placenta, abnormal cardiotocography, or prolapsed cord. Women who did not receive ACS because of major congenital anomalies, a gestational age, or estimated fetal weight below viability were included in the indication poor prognosis. Advanced delivery included women with advanced cervical dilatation. All cases that could not be included in one of these categories and without a clear reason for not administering ACS in the medical chart, were categorized as no specific reason. Outcome measures were: number of women who received ACS and delivered within 7 days after ACS administration and the time interval between ACS administration and delivery with different indications.

Statistical analysis

Statistical analysis was performed using SPSS software version 20.0 (IBM Corporation, Armonk, NY). We counted the number of women delivering $\leq$7 days and >7 days after ACS administration. Pearson χ^3 tests and independent sample *t* tests were used to evaluate whether there was a significant difference in characteristics between the groups. The median time from the first ACS administration to delivery was calculated for the different indications. A Kaplan-Meier plot was made to express time to delivery per indication. Data were censored after 30 days, because there is no beneficial effect of ACS expected anymore after this period. The study was approved by the medical ethical committee of the participating hospitals.

Results

During the study period 90,248 women delivered in the participating hospitals of the region Utrecht.

The total number of women who received ACS from 2005 until 2010 in the

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