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Steroids during late preterm labor: Better later than never

Steroids—even when administered in the last leg of the late preterm period—still reduce the likelihood of respiratory complications in newborns.

PRACTICE CHANGER

Use steroids in women at risk of preterm delivery, even if they are 36 weeks, 6 days' pregnant, because steroids may reduce respiratory complications in the newborn with minimal risk for neonatal or maternal complications.

Gyamfi-Bannerman C, Thom EA, Blackwell SC, et al; NICHD Maternal–Fetal Medicine Units Network. Antenatal betamethasone for women at risk for late preterm delivery. *N Engl J Med*. 2016;374:1311-1320.[1]

STRENGTH OF RECOMMENDATION

A: Based on a good quality randomized controlled trial and consistent with a meta-analysis.

ILLUSTRATIVE CASE

A 21-year-old G1P0 at 35 weeks, 2 days of gestation presents to labor and delivery reporting a "gush of clear fluid." On exam, you confirm she has preterm rupture of membranes. She is contracting every 3 minutes and has a cervix dilated to 3 cm. Is there any neonatal benefit to providing corticosteroids in this late preterm period?

Approximately 12% of all births in the United States are the result of preterm labor,[2] and 8% are born in the late preterm period, defined as 34 to 36 weeks' gestation.[3] To reduce the risk of neonatal death and respiratory complications, both the American College of Obstetricians and Gynecologists and the National Institutes of Health recommend a course of corticosteroids between 24 and 34 weeks' gestation for women at increased risk of preterm delivery.[2,4] Due to a lack of evidence from randomized controlled trials (RCTs) on the benefit of corticosteroids in late preterm labor, there have not been recommendations to extend this period.[5] However, multiple studies have shown that babies born during the late preterm period have more neonatal complications than term newborns.[6-8]

A retrospective chart review of more than 130,000 live births found newborns delivered between 34 and 36 weeks had higher rates of respiratory distress than those delivered at 39 weeks (ventilator use dropped from 3.3% at 34 weeks to 0.3% at 39 weeks and transient tachypnea decreased from 2.4% at 34 weeks to 0.4% at 39 weeks).[6] Another retrospective review of more than 230,000 newborns, of which 19,000 were born in the late preterm period, revealed that more neonates born between 34 and 36 weeks' gestation had respiratory distress syndrome than neonates delivered at 39 weeks (10.5% at 34 weeks, 6% at 35 weeks, 2.8% at 36 weeks vs 0.3% at 39 weeks; $P<.001$ for the trend).[8]

STUDY SUMMARY

Late preterm newborns breathe better with antenatal betamethasone

This randomized placebo-controlled trial examined the effectiveness of betamethasone in preventing neonatal respiratory complications for 2831 women at high probability of preterm delivery between 34 weeks and

36 weeks, 6 days of gestation. "High probability of preterm delivery" was defined as preterm labor with intact membranes and at least 3 cm dilation or 75% cervical effacement; spontaneous rupture of membranes; or anticipated preterm delivery for any other indication either through induction or cesarean section between 24 hours and 7 days after the planned randomization.

Patients were randomly assigned to receive either 2 intramuscular injections (12 mg each) of betamethasone or placebo, 24 hours apart. The 2 doses were successfully given in 60% of the betamethasone group and 59% of the placebo group. In 95% of the cases where the second dose was not given, it was because delivery occurred within 24 hours of the first dose.

The primary outcome was the need for respiratory support within 72 hours of birth, which was defined as one or more of the following: the use of continuous positive airway pressure (CPAP) or high-flow nasal cannula for at least 2 consecutive hours, supplemental oxygen for at least 4 continuous hours, extracorporeal membrane oxygenation (ECMO), or mechanical ventilation.

The median time to delivery from enrollment was 31 to 33 hours, and 31.4% underwent cesarean delivery. In the intention-to-treat analysis, the primary outcome was significantly lower in the betamethasone group than in the placebo group (11.6% vs 14.4%; relative risk [RR]=0.80; 95% CI, 0.66-0.97; *P*=.02; number needed to treat [NNT]=35). Secondary outcomes (severe complications, representing a composite of the use of CPAP or high-flow nasal cannula for at least 12 continuous hours, supplemental oxygen for at least 24 continuous hours, ECMO, mechanical ventilation, stillbirth, or neonatal death within 72 hours after delivery) were also lower in the betamethasone group (8.1% vs 12.1%; RR=0.67; 95% CI, 0.53-0.84; *P*<.001; NNT=25). The betamethasone group also had a lower risk of transient tachypnea of the newborn (6.7% vs 9.9%; RR=0.68; 95% CI, 0.53-0.87; *P*=.002).

There were no significant differences in the occurrence of maternal chorioamnionitis (about 2%) or endometritis (about 1%) between the groups. Hypoglycemia in the newborn occurred more in the betamethasone group (24% vs 15%; RR=1.6; 95% CI, 1.37-1.87; *P*<.001; number needed to harm [NNH]=11). The betamethasone group had 2 neonatal deaths: one from septic shock and the other from a structural cardiac anomaly and arrhythmia.

WHAT'S NEW

Betamethasone makes a difference even in the late, late preterm period

This study demonstrated clear benefit in neonatal respiratory outcomes when betamethasone vs placebo was used in the late preterm period. The findings were similar to those from the Antenatal Steroids for Term Elective Caesarean Section Research Team.[9] Their trial showed a reduction in respiratory complications in term neonates delivered via elective cesarean section to mothers who received antenatal betamethasone (NNT=37 to prevent admission to a special care nursery with respiratory distress). The findings were also consistent with those of a recent meta-analysis (including this trial) evaluating the occurrence of respiratory complications with the use of antenatal betamethasone in women expected to deliver in the late preterm period or with a planned cesarean delivery at ≥37 weeks' gestation.[10]

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CAVEATS

Neonates may develop hypoglycemia

The authors of the study reported an increased risk of hypoglycemia in the neonates receiving antenatal betamethasone. The long-term implications of this are unclear, however, given that there was a reduction in intermediate care nursery and neonatal intensive care unit stays that were 3 days or longer in the betamethasone group. Also, there was no difference in hospital length of stay between the 2 groups. In addition, it's not clear if there are any long-term neonatal complications of betamethasone use in the late preterm period.

CHALLENGES TO IMPLEMENTATION

Challenges are negligible since betamethasone is readily available

There are minimal challenges to implement-

ing this strategy, as betamethasone is routinely used for preterm labor and is readily available on labor and delivery units. JFP

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