

Antenatal Corticosteroids for Fetal Benefit in the Preterm Period

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BACKGROUND

Antenatal corticosteroids are one of the most important antenatal therapies to improve neonatal outcomes. Antenatal steroids are a course of maternal steroid injections given over a two-day period to temporarily expedite fetal lung maturity and reduce the risk of other serious neonatal complications such as intraventricular hemorrhage, necrotizing enterocolitis, and all-cause mortality in situations where preterm delivery is anticipated. Maximum fetal benefit is achieved if antenatal corticosteroids are administered one to seven days prior to preterm birth. There is minimal efficacy when antenatal corticosteroids are administered within 24 hours of birth, and the efficacy of antenatal corticosteroids decreases seven days following administration.

In the early preterm period (before 34 0/7 weeks), antenatal steroids are routinely recommended when there is risk for preterm delivery within the next seven days. In the late preterm period (34 0/7 weeks – 36 6/7 weeks), the potential benefits decrease as the fetus approaches the early term period. As such, late preterm administration is often a shared decision, weighing time and route of delivery, concerns for maternal blood sugar control or infection, and other considerations.

ELIGIBILITY

Pregnancy at increased risk of preterm birth within the next seven days.

INDICATIONS FOR INITIAL COURSE OF ANTENATAL CORTICOSTEROIDS IN SINGLETON PREGNANCIES

PREVIABLE: 20 0/7 weeks – 21 6/7 weeks

- Antenatal corticosteroids are not recommended.

PERIVABLE: 22 0/7 weeks – 23 6/7 weeks

- Consider antenatal corticosteroids (dose below).

PRETERM: 24 0/7 weeks – < 33 6/7 weeks

- One standard course of antenatal corticosteroids
 - Betamethasone 12 mg IM, q 24 hours x 2 doses or
 - Dexamethasone 6mg IM q12 hours, x 4 doses if betamethasone is unavailable.
 - If initiated at an outside facility, the full corticosteroid course should be continued with the same medication that was initiated.

LATE PRETERM: 34 0/7 weeks – ≤ 36 6/7 weeks

- Administration of late preterm corticosteroids began following the ALPS (Antenatal Late Preterm Steroid) Trial, which demonstrated that neonates exposed to corticosteroids in the late preterm period had a 20% risk reduction of composite respiratory outcome.
- Since that original study, many others have been conducted to further evaluate the use of antenatal corticosteroids in the late preterm period.
- In general, shared decision making with the patient should be used and risks/benefits discussed, as someone at 34wks anticipating a cesarean delivery may benefit more than another at 36wks anticipating a vaginal delivery.
- The same dose of antenatal corticosteroids as detailed above is used.

- Delivery, if indicated, should not be delayed for administration of corticosteroids (e.g. preeclampsia with severe features, preterm labor, PPROM, etc). Additionally, tocolysis should not be administered.
- Possible indications for late preterm antenatal corticosteroids:
 - Patient developing preeclampsia or worsening hypertension necessitating earlier delivery.
 - Preterm labor with uterine contractions and cervical change (e.g. dilation of 3 cm or greater, effacement of 75% or greater) or preterm prelabor rupture of membranes (PPROM).
 - Other medical or obstetric conditions that may require delivery in the late preterm period such as bleeding placenta previa, placenta accreta, prior classical uterine incision, intrahepatic cholestasis of pregnancy, fetal growth restriction with abnormal Doppler flow, etc.
- Late preterm antenatal corticosteroids are not recommended if any of the following conditions are present:
 - Concern for intraamniotic infection.
 - Patients with pregestational diabetes (type I or type II).
 - Patients who previously received a course of corticosteroids in the pregnancy.
- There is uncertain benefit for patients with multifetal gestation or fetal anomalies.
- Notify Pediatrics team, as the infant may be at increased risk of neonatal hypoglycemia.

INDICATIONS FOR A SECOND (RESCUE) COURSE OF ANTENATAL CORTICOSTEROIDS

- A repeat course should be considered in patients who have already received a course of corticosteroids that was administered at least seven, but typically 14, days previously, and are between 24 0/7 weeks and ≤ 33 6/7 weeks.
 - In the setting of PPROM, there is a potential lack of benefit and increased risk for maternal harm (endometritis). MFM should be consulted.
- More than one repeat course should not be administered.
- Late preterm pregnancies (34 0/7 weeks – ≤ 36 6/7 weeks) are not candidates.

BENEFITS AND RISKS OF ANTENATAL CORTICOSTEROIDS IN SINGLETON PREGNANCIES PRIOR TO 34 0/7 WEEKS

- Fetal Benefits:
 - Improved fetal lung maturation resulting in decreased respiratory distress syndrome (RDS).
 - Decreased risk of intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC), sepsis, and periventricular leukomalacia.
 - Lower all-cause fetal morbidity and mortality.
- Fetal Risks:
 - Neonatal hypoglycemia.
 - Transient decrease in FHR variability.
 - Transient improvement in umbilical artery end-diastolic flow.

LATE PRETERM PERIOD: 34 0/7 WEEKS – < 36 6/7 WEEKS

- Some studies identify no change in neonatal respiratory support when compared with placebo and others saw no decrease in neonatal death, stillbirth, or severe neonatal respiratory distress.
- Risks and benefits are similar to those noted above.

MATERNAL RISKS

- Transient hyperglycemia or leukocytosis, injection site reaction, pain, uterine irritability, and hyperactivity.
- For patients with gestational diabetes, careful counseling on risks/benefits of corticosteroids followed by close monitoring of blood glucose levels.

CONTRAINDICATIONS TO ANTENATAL CORTICOSTEROIDS

- Hypersensitivity to any component of the medication.
- Use caution in those with systemic infections.

ANTENATAL CORTICOSTEROIDS IN MULTIFETAL GESTATIONS

- MFM consultation recommended as data is still emerging.

PRIOR TO 34 0/7 WEEKS

- Indications are similar to those of singleton pregnancies.

LATE PRETERM PERIOD: 34 0/7 WEEKS – < 36 6/7 WEEKS

- Multiple studies have identified no clear reduction in respiratory morbidity
 - Benefits:
 - Lower risk for supplemental oxygen use and mechanical ventilation.
 - Improved short-term neurologic outcomes.
 - Risks:
 - One study by Yenuberi noted higher rate of NICU admission for hypoglycemia but not hypoglycemia in general.
 - Another study by Vieira identified increased rates of neonatal hypoglycemia.

LONG-TERM CHILDHOOD OUTCOMES AFTER ANTENATAL CORTICOSTEROID ADMINISTRATION

- In general, long-term risks are still uncertain. There is inconsistent evidence to definitively state that antenatal corticosteroids affect long-term neurodevelopmental outcomes such as autism spectrum disorders, attention-deficit hyperactivity disorder, mood, or anxiety disorders.

PRIOR TO 34 0/7 WEEKS

- No evidence of increased risk of abnormal childhood neurodevelopment.

LATE PRETERM PERIOD

- Lower rates of wheezing or whistling in the chest without differences in other respiratory outcomes (asthma, abnormal spirometry, pneumonia).

MULTIPLE COURSES OF CORTICOSTEROIDS

- Reduced fetal growth and neonatal head circumference.
- No difference noted in children at two years of age.

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