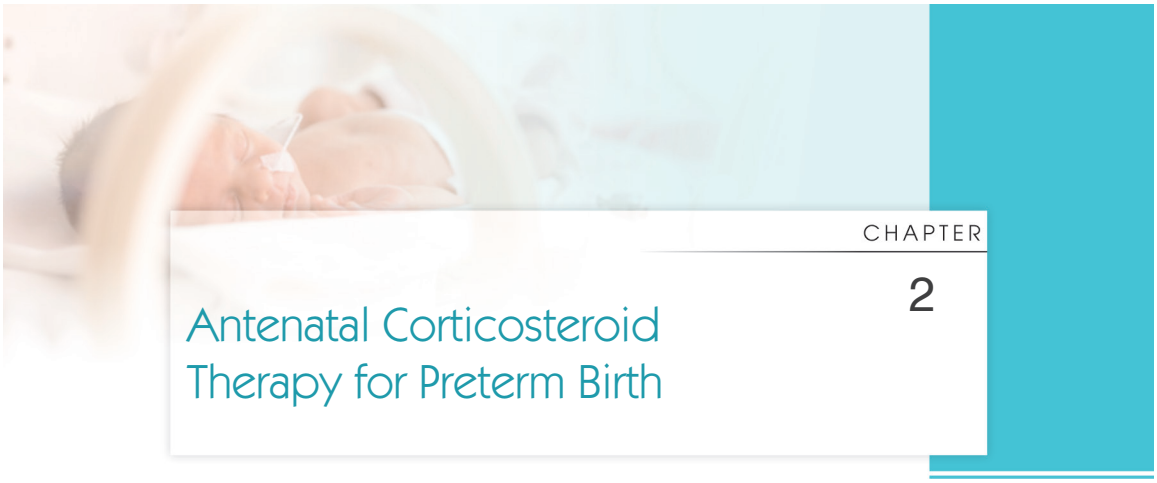

CHAPTER

2

Antenatal Corticosteroid Therapy for Preterm Birth

Globally, complications of preterm birth are the leading cause of under-5 mortality, accounting for 20% under-5 deaths in 2015.[1] Preterm infants who survive are at a risk of wide range of morbidities. Administration of antenatal corticosteroids (ACS) to mother for enhancing fetal lung maturity before any anticipated preterm birth is one of the most important strategies to improve the preterm neonatal outcomes.

BENEFITS

The updated Cochrane (2020) reaffirms the reduction of perinatal death, neonatal death, respiratory distress syndrome and intraventricular-periventricular hemmorhage by 15% (RR 0.85, 95% CI 0.77–0.93), 22% (RR 0.78, 0.70–0.87), 29% (RR 0.71, 0.65–0.78) and 42% (RR 0.58, 0.45–0.75), respectively.[2]

FIRST COURSE

We give the first course of ACS therapy in women at risk of preterm birth from 24^{+0} weeks to 34 weeks of gestation (irrespective of singleton or multiple pregnancy and the growth restriction of the fetus) when all the following conditions are met:[3]

i. Gestational age assessment can be accurately undertaken
ii. Preterm birth is considered imminent as evidenced by onset of true labor pains
iii. There is no clinical evidence of maternal infection

It is important that health facilities providing ACS therapy to women with preterm labor has adequate childbirth care including the capacity to recognize and manage preterm labor and birth and the preterm newborn can receive adequate care (including resuscitation, thermal care, feeding support, infection treatment and safe oxygen use).

There is variation in the recommended gestation range for administration of the first course of ACS: ACOG 2017[4] and NICE 2016[5] recommend this gestation range as 24^{+0} to 33^{+6} weeks while WHO[3] and Government of India as 24–34 weeks of gestation.

Drugs and Dosage[3]

Two drugs can be used for ACS therapy:

1. **Dexamethasone:** 6 mg every 12 hours for a total of 4 doses (24 mg).
2. **Betamethasone:** a mixture (1:1) of betamethasone acetate (long acting) and betamethasone phosphate (fast acting): 12 mg every 24 hours, a total of 2 doses (24 mg).

As the combination preparation of betamethasone is not available in India (the available preparation is betamethasone phosphate) and is costly as an imported product, dexamethasone is the drug of choice given its comparable efficacy and safety, wide availability, and low cost.[6]

i. Give the first dose of ACS in imminent delivery. Even a single dose given within 24 hours of delivery is associated with significant reduction in neonatal morbidity and mortality.[3]
ii. Multiple fetal pregnancies (twins, triplets) should receive the same dose as singleton.[3]
iii. Mothers diagnosed with pregestational and gestational diabetes should be administered complete course of ACS. Interventions to optimize the maternal blood glucose levels should be ensured.[3]
iv. Mothers already on oral steroids like prednisolone should also receive the standard course of ACS.

Contraindications

Chorioamnionitis is the only absolute contraindication. Maternal diabetes, preeclampsia and hypertension are **NOT** contraindications for using ACS.

Repeat Course

Consider a repeat course in women with:

a. Pregnancy of less than 34^{+6} weeks
b. Still at risk of preterm labor within next 7 days, and
c. Prior dose of ACS given more than 14 days ago.[4]

Only single repeat course is recommended, avoid multiple courses.

Interval between the first course and repeat course is still debatable. WHO recommends it to be 7 days instead of 14 days.[3] RCOG and Government of India guidelines, 2014 do not recommend the repeat course.

Late Preterm ($34^{0/7}$ to $36^{6/7}$ Weeks)

We do not use ACS in late preterm of $34^{0/6}$ to $36^{6/7}$ weeks' gestation.

Current evidence does not support use of ACS in late preterm pregnancies. A systematic review[7] showed short-term benefits in neonatal morbidities: lower risk of transient tachypnea of the newborn (RR 0.56, 95% CI 0.37–0.86), severe RDS (0.55, 0.33–0.91), use of surfactant, and mechanical ventilation, and lower time of receiving oxygen, and a shorter duration of stay in NICU. However, there was no difference in neonatal mortality. WHO and Government of India guidelines recommend against the administration of corticosteroids for lung maturity beyond 34 weeks of gestation.

Periviable Gestation (22–24 Weeks)

The decision to administer corticosteroids in gestation below 24 weeks should be individualized considering the neonatal unit's capability to provide care to such babies and parental wishes.

Evidence supports the benefits of ACS in preterm neonates born at 22–24 weeks' gestation. A meta-analysis showed reduced mortality (OR 0.48; 95% CI 0.42–0.55) and peri-intraventricular hemorhage and periventricular leucomalacia (OR 0.70, 95% CI 0.63–0.79) in these neonates.[8]

Elective Cesarean Sections in more than 34 Weeks' Gestation

ACS is not recommended in women undergoing planned cesarean section at late preterm gestations (34–36^{+6} weeks)

Table 2.1: Guideline recommendations for antenatal corticosteroids

RCOG Updated August 2021

1. Clinicians should offer a single course of antenatal corticosteroids to women between 24^{+0} and 34^{+6} weeks of gestation who are at risk of preterm birth.
2. Antenatal corticosteroids can be considered for women between 23^{+0} and 23^{+6} weeks of gestation who are at risk of preterm birth.
3. The decision to administer corticosteroids at gestations less than 24^{+0} weeks should be made at a senior level taking all clinical aspects into consideration.
4. Antenatal corticosteroids should be given to all women at risk of iatrogenic or spontaneous preterm birth up to 34^{+6} weeks of gestation.

(*Contd.*)

Table 2.1: Guideline recommendations for antenatal corticosteroids (*Contd.*)

5. Senior opinion should be sought if a rescue course is to be considered. A rescue course of two doses of 12 mg betamethasone or four doses of 6 mg dexamethasone should only be considered with caution in those pregnancies where the first course was given at less than 26^{+0} weeks of gestation and another obstetric indication arises later in pregnancy.

ACOG 2017

1. A single course of corticosteroids is recommended for pregnant women between $24^{0/7}$ weeks and $33^{6/7}$ weeks of gestation who are at risk of preterm delivery within 7 days, including for those with ruptured membranes and multiple gestations. It also may be considered for pregnant women starting at $23^{0/7}$ weeks of gestation who are at risk of preterm delivery within 7 days, based on a family's decision regarding resuscitation, irrespective of membrane rupture status and regardless of fetal number.
2. A single course of betamethasone is recommended for pregnant women between $34^{0/7}$ weeks and $36^{6/7}$ weeks of gestation at risk of preterm birth within 7 days, and who have not received a previous course of antenatal corticosteroids.
3. Regularly scheduled repeat courses or serial courses (more than two) are not currently recommended.
4. A single repeat course of antenatal corticosteroids should be considered in women who are less than $34^{0/7}$ weeks of gestation who are at risk of preterm delivery within 7 days, and whose prior course of antenatal corticosteroids was administered more than 14 days previously. Rescue course corticosteroids could be provided as early as 7 days from the prior dose, if indicated by the clinical scenario.

WHO September 2022

Antenatal corticosteroid therapy is recommended for women with a high likelihood of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met.

1. Gestational age assessment can be accurately undertaken.
2. There is a high likelihood of preterm birth within 7 days of starting therapy.
3. There is no clinical evidence of maternal infection.
4. Adequate childbirth care is available (including capacity to recognize and safely manage preterm labour and birth).
5. The preterm newborn can receive adequate care (including resuscitation, kangaroo mother care, thermal care, feeding support, infection treatment and respiratory support including continuous positive airway pressure [CPAP] as needed).

Antenatal corticosteroid therapy is not recommended for women undergoing planned caesarean section at 34 weeks 0 days to 36 weeks 6 days.

A single repeat course of antenatal corticosteroids is recommended for women who have received a single course of antenatal corticosteroids at least 7 days prior and, on clinical assessment, have a high likelihood of giving birth preterm in the next 7 days.

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